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THE IMPORTANCE OF BASAL BLOOD PRESSURE

JOHN R. CALDWELL, M.D.*
F. WAYNE HOLLINGER, M.D.**

1. *Introduction*

It has been said that the sphygmomanometer is an "instrument of the devil," that "the worst way to find out what a patient's blood pressure is, is to take it," that "a single recorded pressure has a validity of about 10 percent."

Personal experience with the vagaries of blood pressure measurement and observations by thoughful physicians lead us to reexamine the significance of occasional blood pressure readings, one of the most widely variable of biological measurements. If the doctor discovers casual blood pressure readings to be within accepted normal range as outlined by Master and associates,[14] and if there is no objective evidence of hypertensive vascular disease on clinical, x-ray, EKG, and laboratory examinations, one can exclude hypertensive disease.

If an elevated blood pressure is found it is important to determine its significance especially since potent and effective antihypertensive agents are now available and the rewards of adequate treatment are gratifying, in properly selected patients.

This paper will be a restatement with new emphasis of facts known but not used enough in practice.

2. *Information from previous studies on Basal blood pressure.*

Thomas Addis,[1] in 1922, emphasized that the significance of any given blood pressure reading or pulse rate depended first on a knowledge of the condition under which the observation was made. He designated as "basal blood pressure" that measurement taken before the subject had risen from bed or taken food. He then specified a "daytime blood pressure" as the pressure taken anytime after subjects had risen from bed and had had food. In all cases readings were taken in the recumbent position after a brief period of rest and without any previous excess muscular exertion.

He found that basal averages of pressure in normal men were considerably lower than daytime averages. In hypertensive young men the average basal blood pressure was higher than in normals. A measure which would be "normal" for the day would be unusually high if it were found under basal conditions.

Addis describes two types of hypertension, (1) with marked fall in basal pressure as contrasted to daytime pressures, and (2) those with only a slight decrease in basal pressure. The latter he felt had a more grave prognosis. In his words, "an average daytime pressure in a patient at 177/97, for example, would be more easily borne than a pressure of 167/107 in a patient with Bright's disease, because in the first case the cardiovascular system is rested each night by the fall to 113/80 whereas in the renal case there is no remission, and the heart has continually to work against a high diastolic pressure."

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The differences in basal and daytime pressures he found to be due to excitement, which increased both systolic and diastolic pressure, exercise, which increased systolic and reduced diastolic pressure and food, which would increase systolic pressure with no significant effect on the diastolic pressure.

Sladen and Johnston[18] of this hospital called attention in 1926 to the significance of basal blood pressure, and most of the conclusions we have made were anticipated 30 years ago by them. Unfortunately, these observations never received the dominant place they deserve in the evaluation of sphygmomanometer readings in clinical practice.

Alam and Smirk[2,3] describe a technique for obtaining lower pressures than with the basal methods alone used by Addis. They accomplished this by desensitizing the patient to sphygmomanometry with frequent recordings over a three minute period, then subsequent readings every few minutes for one-half hour. The patient was sitting in a warm quiet room with no special regard to the time of day, or to meals. In a group of 27 patients with essential hypertension, the average casual blood pressure was 195/116 and the average basal pressure was 151/95. These levels were reached after 2 to 4 hours of rest and habituation to the observer, and the sphygmomanometer.

Basal blood pressure obtained by this method corresponds well with results of basal recordings in patients whose pressure was checked prior to rising or taking food.[17]

Repeated basal blood pressure readings were performed by Kilpatrick[4] daily for 4 to 7 days in a group of patients. Eleven had normal casual pressures. Eight were so called "prehypertensive" and fourteen were hypertensive. Basal systolic pressures were quite constant from day to day in the normotensives and basal diastolic pressure generally followed the same pattern. Frequently the first basal pressure was higher than subsequent basal readings.

In the prehypertensive or hyperreactor group basal blood pressure was more variable than in normals. This also was true of hypertensive patients. However, the mean basal levels of vascular hyperreactors or "prehypertensives" were not significantly higher than in normotensives. Patients with sustained hypertension and evidence of cardiac enlargement by x-ray in Alstad's[5] experience showed in general higher basal pressures associated with higher casual pressures. High basal pressures occurred in those with fixed hypertension and more advanced arterial pathological changes.

Kilpatrick[4] also studied 44 cases comparing one casual blood pressure with one basal blood pressure. The casual blood pressures were uniformly higher than basal pressures and the difference between the two was termed "supplemental blood pressure." In normotensives the mean systolic supplemental blood pressure was 18 mm. Hg. In "prehypertensives" it was 25mm. Hg. In the hypertensive group supplemental pressure was 44 mm. Hg. and in hypertensives with congestive heart failure 9 mm. Hg. Since the mean supplemental pressure was significantly higher in the hypertensive group than in the normals this indicates the wide and exceedingly variable range of casual pressures in patients with essential hypertension. Low supplemental pressures were found to occur in heart failure and chronic nephritis. Thirty-two patients with hypertensive cardiovascular disease showed an average supplemental blood pressure of 48/22 mm. Hg. in a study by Alstad.[5] Kilpatrick[4] concluded that basal blood pressure of normal subjects is constant over observed periods of one to three weeks while casual blood pressure of normals is variable.

Casual pressures of patients with essential hypertension are exceedingly variable, whereas, basal blood pressure in these patients is more constant. Concealed emotional factors produced remarkable divergences from the usual basal level in some cases. It was observed that in many patients with essential hypertension there was greater difficulty in obtaining basal conditions than in normotensive patients.

3. *Variations in blood pressure according to different examiners and environment.*

Most physicians are aware of the effect of excitement and tension associated with the visit to the clinic or doctor, and with the differences in blood pressure obtained by different individuals. Still the common method of recording blood pressure appears to be for the physician to determine a single initial reading without rest.

The striking differences in blood pressure readings by the physician in his office and by non-professional personnel in another environment was pointed out by Ayman and Goldshine[6] in 1940. In their patients with essential hypertension home pressure readings by the patient or a member of the family were lower than those obtained in the clinic by the doctor. The greatest differences between home and clinic readings were found when the determinations were done before resting. Different individuals in the home got different readings on one patient. A high strung talkative daughter got higher recordings than a calmer, more relaxed daughter. In 30% of their patients averages of systolic home recordings were 40 mm. Hg. lower than in the clinic. In 23% averages of diastolic home pressures were 20 mm. Hg. lower than in the clinic by the doctor. Ayman observing these differences between home and clinic readings thought that these facts should help many physicians understand why some of their supposedly severe hypertensive patients have lived many years. We are all familiar with the occasional patient that has had "blood pressures of over 200 mm. Hg." and lives 20 years without apparent difficulty. Yet this patient may well have had pressures of 140 or less except when visiting a physician or in a momentary period of excitement.

The marked discrepancy between home and office recorded pressures led Freis[7] to observe that the physician depending only on office recordings in patients under treatment with pentapyrollidinium would be unable to recognize the point at which a therapeutic dose level had been obtained. He also emphasized that the visit to the doctor was a pressor stimulus of such magnitude that the hypotensive effects of the drug were frequently overcome. He presented evidence that excessively high office pressures while under treatment were due to escape from the hypotensive effects of the drug during the time the patient visited the office or clinic.

Our experience with the use of ganglionic blocking agents has been such that we find it impossible to regulate adequately patients' blood pressure with these drugs without home recordings as a guide.

Recently Corcoran[8] has shown that the most stable levels of blood pressure are obtained by averaging hospital recorded pressures and averaging weekly home recorded pressures. There was noted in his series good correlation between these two figures. The blood pressure determinations in the averages he obtained were not made by physicians. He also reported the wide discrepancy in clinic and home recorded pressures and suggested the use of mean hospital and home pressures in an approach to evaluation of the effectiveness of an antihypertensive agent. Many of the misleading claims regarding the effectiveness of antihypertensive drugs are due to reliance on casual office recorded pressures by physicians. In comparative blood pressure studies before and after sympathectomy Whitelaw and Smithwick[16] emphasize time and again that

these studies should not be done in a doctor's office or by a doctor. Rather, they should be done in a quiet room under standard conditions by a competent technician.

At routine office visits we have had a technical assistant or office nurse check the patient's blood pressure on arrival according to standard precedures for sphygmomanometry.[10] The physician repeats the blood pressure determination after his interview. By doing this we have noted surprisingly large differences in some patients between the blood pressure as recorded by the nurse or technical assistant and the doctor (See Table I). This has brought home to us the striking differences in blood pressure levels which are obtained by different examiners. These differences are much more marked than one would expect as due to the usual range of error of + or — 8 mm. Hg. due to sphygmomanometric technique.

Table I
CASUAL OFFICE BLOOD PRESSURE
Mercury Manometer

NAME	CASE No.	DATE	B. P. BY TECHNICIAN OR NURSE	B. P. 5-15 Minutes LATER BY PHYSICIAN
J. R.	037147	6-8-55	140/80	170/80
E. A.	781746	5-20-55	160/110	140/90
J. O.	095741	7-11-55	200/98	210/110
I. A.	793339	6-20-55	220/120	210/96
J. Y.	352953	4-19-55	120/50	140/70
A. W.	238486	5-24-55	140/86	170/100
N. B.	620755	6-14-55	200/112	230/130
D. S.	786216	6-21-55	180/100	168/96
S. M.	587373	4-1-55	150/112	190/120
Z. H.	158395	4-20-55	160/100	190/110
M. B.	326394	5-12-55	210/104	190/100
M. H.	763660	5-25-55	134/80	140/90
F. H.	755771	6-22-55	152/96	190/110
H. S.	794040	6-14-55	190/130	200/140
E. G.	566186	6-23-55	134/74	128/70
R. B.	777138	7-2-55	184/88	200/100
J. C.	392630	7-19-55	136/84	150/94
W. H.	213075	7-18-55	224/144	224/160
F. R.	786614	7-20-55	188/96	210/100
R. M.	778657	6-1-55	190/106	220/120
M. B.	552708	6-17-55	156/84	156/88
J. M.	793421	6-24-55	164/90	164/90
C. M.	261495	7-5-55	170/86	200/100
R. B.	698883	7-22-55	226/80	240/90
A. K.	794920	7-22-55	190/100	174/90
E. R.	325895	7-22-55	140/78	130/80
A. T.	779460	7-22-55	154/86	158/90
K. S.	653747	7-17-55	160/90	170/108
M. E.	500675	4-18-55	175/110	150/100
K. L.	556195	7-22-55	190/118	200/120
M. O.	733728	5-18-55	210/110	200/110
B. K.	768833	6-15-55	154/90	170/96
A. F.	095317	7-28-55	182/90	170/90
E. H.	212355	7-28-55	160/110	145/90
M. M.	776484	7-28-55	190/108	200/120
H. B.		7-19-55	140/72	140/70
S. T.	491434	7-28-55	124/78	100/70

By plotting out the readings on Table I in a dot graph (Fig. 1) it can be shown that dots above the diagonal line represent higher readings by the physician on routine office visits than those obtained by the nurse. Conversely, those dots below the diagonal line indicate instances in which the doctor's reading was the lower of the two. This may be due to physical or emotional rest while relaxing in the waiting room or to any of a wide number of diverse factors in the doctor-patient relationship, but nevertheless, it points up the variability of response to different observers.

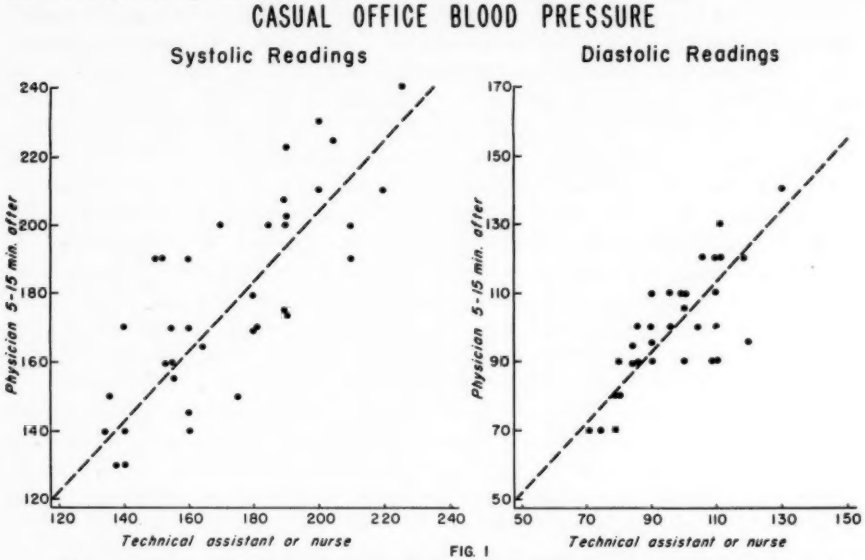


FIG. 1

Discussion by some patients regarding the phenomena of different readings by different individuals has yielded some interesting explanations.—"I believe the younger and more intense or more interested doctors get higher readings. The older doctors don't seem to care so much what it is and get lower readings." Another patient says, "When I see the doctor and begin to talk over my problem, then I believe my pressure goes up. Just thinking about . . . gets me upset and when I see the doctor I must think and talk about this problem."

Fear that the doctor with his knowledge of disease may make a dire prognostic interpretation of a reading he takes may elevate the blood pressure. One patient who was rejected for life insurance because of elevated blood pressure had normal readings when checked by the nurse, but much higher when checked by the doctor. He said, "I wasn't paying much attention when the nurse took my blood pressure, but when the doctor did, I figured—this is what counts."

Difference in blood pressure of normotensive and healthy young men to two examiners in otherwise identical experimental situations have been demonstrated by Reiser and associates.[11] This phenomena, in milder degree, is not confined to patients with known vascular hyperreactivity or established hypertensive disease.

We have noted that many patients who show a pressor response to readings by a physician are totally unaware of this psychic influence and show little visible emotional response to accompany the difference in reading found.

It may well be that the derided fakirs who set up shop as blood pressure specialists in penny arcades evoke sometimes less pressor response than the physician. Certainly such pressure records for 50 cents on passerbys in the streets are worthless in view of the exercise and non-basal conditions. But conceivably they could be less pressor-like than an emotionally tinged visit to a physician in a setting of authority in which great importance is placed on the presence or absence of serious illness and its possible consequence to the patient.

Because blood pressure is so variable and may be influenced by emotional tension, excitement, reactions to different examiners and environs, exercise, food, temperature, etc., it should prove valuable to obtain basal blood pressures with an automatic recording device which would separate the patient clearly from the examining physician or nurse to eliminate this variable of the response of the subject to the examiner.

4. *Method*

Our method for obtaining basal blood pressure as we use the term would perhaps more precisely be called resting daytime blood pressure. Our aim is to determine levels of blood pressure at a time when the patient has a minimum of mental and emotional stimuli and a minimum of physical and metabolic activity. These patients are not in a basal metabolic state since this requires considerable inconvenience and since levels of blood pressure just as low as those obtained under truly basal conditions can be achieved by emotional desensitization to sphygmomanometry when the test is done in an atmosphere of friendliness and tranquillity favoring relaxation.

It is a modified form of the Alam-Smirk method,[2,3] and is especially convenient and practical for use in the out-patient clinic or office. We do not use a sedative prior to the test since it has been shown by Winchell and associates[12] that sodium amytal decreases cardiac output without reducing peripheral resistance, but prefer to rely on minimum physiological pressure readings.

The patient is seen on appointment by our technical assistant expressly for the purpose of obtaining resting or basal blood pressure. The attending physician is not seen at this visit or if so only in a casual manner. The patient is placed recumbent in a large, warm and quiet room on a comfortable cot. The technician places a "Do Not Disturb" sign outside the door of the room, enters quietly and assumes a friendly and sedate manner toward the patient. Adjusting the sphygmomanometer she proceeds to record the blood pressure rapidly and frequently over the first three minutes to "desensitize the patient to sphygmomanometry."[2] Thereafter the blood pressure is determined every five minutes for a period of one-half hour. All blood pressure measurements are made on the same arm at heart level with the same mercury manometer using the method of judging systolic and diastolic level as detailed by the American Heart Association recommendations of 1951.[10]

5. *Observations*

Usually the lowest pressures are obtained after about 10 or 20 minutes and this we designate as the basal blood pressure. After the 30 minute rest period if the basal blood pressures are not unduly high we may then decide to do a standard cold pressor test, after the method of Hines and Brown.[15]

With our method for obtaining "basal" blood pressures we have been impressed by the fact that the lowest pressures attained are often much lower than were observed at the initial clinic visit. They aid us to separate the "transient hypertensives" who have shown a "psychic pressor effect" from those with sustained hypertension.

We have noted that sometimes the maximum height of blood pressure on cold pressor test has not been as high as the first reading of blood pressure in our out-patient department by a physician. (See Table II). This has been described by Hines.[13] The first reading of a patient's blood pressure by a physician with whom the patient is unacquainted and in unfamiliar surroundings may represent the individual's vasomotor reaction to nervous tension and is in effect a psychic pressor test.

Table II

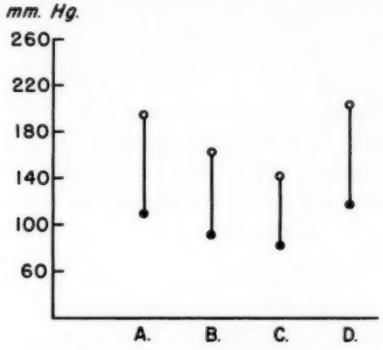
NAME	CASE No.	DATE OF BASAL	CASUAL B. P.*	BASAL BLOOD PRESSURE# HIGH	LOW	COLD PRESSOR HIGH
F. H.	755771	2-28	190/120	160/94	142/90	210/102
K. M.	777227	2-16	180/90	144/90	130/84	160/102
J. B.	781291	2-24	200/110	190/104	170/104	200/110
A. P.	669215	2-25	200/120	220/110	180/100	240/130
H. H.	606079	3-1	194/90	170/70	160/60	200/70
L. J.	781444	3-1	224/118	200/90	170/90	220/94
M. V.	623169	2-28	195/100	184/96	160/90	210/110
E. C.	779356	3-1	200/120	170/94	140/94	220/120
D. B.	774259	3-8	150/90	160/98	140/90	180/110
A. B.	597347	4-4	180/110	160/102	156/90	200/120
L. C.	726416	4-4	180/110	148/88	138/80	160/100
F. H.	785027	4-1	170/110	170/100	154/102	180/114
G. B.	781183	3-16	190/120	150/94	140/100	180/120
D. S.	785494	4-6	160/120	154/90	134/84	190/140
M. M.	403762	4-11	220/120	160/90	160/100	210/118
W. F.	303788	4-11	192/110	160/84	150/82	200/110
C. B.	785761	4-7	160/110	140/80	120/80	160/108
A. H.	551734	4-5	160/115	170/112	140/108	190/122
M. M.	776484	4-19	210/120	150/80	130/80	170/104
C. L.	783522	3-23	190/100	190/100	170/80	220/120
D. S.	580871	4-12	210/150	220/150	170/110	230/200
I. A.	132702	3-31	190/110	160/88	140/86	210/118
B. W.	788216	4-27	165/110	160/88	130/100	190/130
M. S.	789041	4-27	200/100	190/100	160/90	190/112
M. B.	326394	5-16	210/104	226/84	160/74	240/100
M. S.	253817	5-23	214/120	198/108	160/90	230/130
H. G.	174600	6-2	160/90	170/90	150/90	230/130
C. B.	718611	6-3	160/94	170/100	158/100	162/110
A. D.	789549	6-8	210/130	180/130	170/120	210/130
J. K.	757083	6-13	164/84	150/78	130/76	150/90
A. H.	230181	6-24	210/110	150/100	140/100	180/124
L. M.	178721	6-21	200/100	150/92	124/86	180/100
E. M.	300898	6-24	140/80	160/86	140/80	240/140
A. G.	792666	6-30	190/100	180/120	170/100	250/150
O. L.	356037	7-6	220/110	160/90	130/80	210/130
R. B.	777138	7-7	200/110	170/90	140/86	210/130
E. R.	325895	7-14	180/100	120/70	110/70	150/100
AVERAGES OF	SYSTOLIC		194	169	148	199
	DIASTOLIC		108	95	90	118

*Casual Blood Pressure here refers to Blood Pressure by physician at most recent complete examination.

#"Basal" here not under basal metabolic conditions nor always according to method outlined in article but varied somewhat in the process of evolving our technique for determining basal blood pressure.

To show the differences in blood pressure readings obtained under these varying conditions we have averaged readings in 37 patients (See Fig. 2). The only factor in selection of these cases was that they were patients seen in the hypertension division on whom we decided to do "basal" and cold pressor tests. "Basal" is in quotation marks because the test was not always done according to the method described here but varied somewhat in the evolution of our method. The averages here charted (Fig. 2) have little meaning other than to show that casual readings may be as high as the induced maximum by cold stimulus and that the "basal" is significantly lower than both.

MAXIMUM AND MINIMUM BLOOD PRESSURES+



A. Casual office blood pressure by physician at time of most recent complete physical exam.

B. Highest (usually initial) reading during "Basal" blood pressure determination.

C. "Basal" Blood Pressure (minimum).

D. Maximum Rise on Cold Pressor Test.

+*Averages from readings on 37 patients seen in Hypertension Division Jan. '55 - Aug '55 without regard to precise diagnosis.*

FIG. 2

6. *Speculations regarding prognosis.*

Hines[13] found that 82% of patients with blood pressure over 140/85 on first visits at Mayo Clinic developed subsequent hypertension within a 20 year followup study. This is highly significant and suggests that individuals who respond with elevation of pressure to the psychic pressor effects of examination and blood pressure recording by a physician will subsequently develop hypertension. Hines' experience with the cold pressor tests led him to believe by this also that hyperreactivity is a precursor to sustained hypertension and should be termed "prehypertensive state." Of course our primary interest is in the 82% and is to detect and treat early those patients who show evidence of hypertensive vascular disease.

We have also been interested in the other 18% who after 20 years did not develop hypertensive vascular disease. This figure corresponds well with the number of normotensive vascular hyperreactors to cold stimulus found by Smithwick and Robertson.[9]

This group of "transient hypertensives" who will not necessarily develop sub-

sequent hypertension attract our attention. Such patients in the absence of objective evidence of vascular damage certainly should not be treated for 20 years or more unnecessarily with drugs which are expensive and may have some disagreeable side effects.

By determining basal blood pressure on patients with elevated blood pressure one is in a much better position to select such patients than can be done by the use of casual office blood pressures alone.

They could perhaps be designated as showing vascular hyperreactivity on the basis of their pressor response to psychic stimulation. This could be evaluated further by cold pressor response. Of course the question of presence or absence of any vascular damage must be determined by complete examination. We do have a number of patients who have had high casual readings for 10 or 20 years who have low basal readings and no objective evidence of cardiovascular disease.

Whether basal blood pressure determinations will give us information of definite prognostic significance we hope to determine in the future.

7. *Evaluation of the pharmacologic effect of antihypertensive drugs.*

For many years it has been known that blood pressure changes of emotional origin have led to unsatisfactory evaluation of the effects of drugs.

Basal blood pressure determinations reduce mental and emotional stimulation to a minimum and reflect more nearly the "fixed level" of blood pressure.

Significant reductions in basal blood pressure on drug treatment would probably more nearly reflect an antihypertensive pharmacologic effect according to Alstad.[5]

Therefore, we have been interested in determining pre-treatment basal blood pressures and observing the changes in basal levels occurring with drug treatment. We believe that this method may give us a more reliable indication of drug effect than reliance on casual pressures. In clinical investigation of drug effects this might

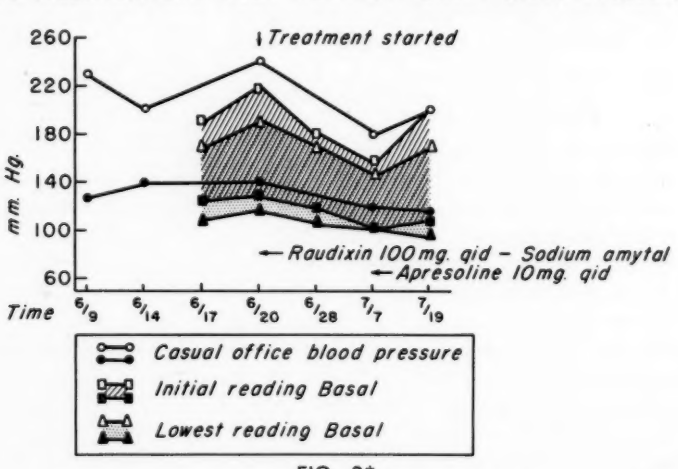


FIG. 3*

*Since this manuscript was submitted for publication this patient has shown continued decline in both basal and casual blood pressure readings. This has been his response to gradual increase in dosage of apresolive to 100 mg. q.i.d. and weight reduction. When examined in October and November he was symptom free and basal and casual pressures ranged from 120/80 to 110/70.

obviate the need for home recordings on patients who do not require ganglionic blocking agents, and at the same time give us a fair appraisal of drug effect. Figure 3 shows such a study in a 65 year old male with hypertensive cardiovascular disease.

8. *Conclusions*

Blood pressure in an individual varies widely under differing environmental conditions and as determined by different examiners. Basal blood pressure is a more constant and a more reproducible index of blood pressure levels than is the customary casual office readings as demonstrated by Kilpatrick.[4]

A practical method for measuring the physiological minimum of blood pressure in the out-patient clinic or office is described. This is of importance because it enlightens both the physician and the patient by demonstrating the range of variability in blood pressure and the value of rest.

As done here it eliminates the pressor aspect of readings by the physician, although this can be achieved very simply by having a nurse or competent technician determine blood pressure at the time of routine office visits.

Basal blood pressure aids in separating "transient hypertensives" or "vascular hyperreactors" from those with sustained hypertension. It gives information regarding the "fixed level" and may prove to be of value in prognosis.

Noting a wide discrepancy between casual and basal levels in some patients with low basal levels, a physician may avoid enthusiastic overtreatment of "vascular hyperreactors." By determination of basal blood pressure before treatment one is in a better position to evaluate psychic factors as contrasted to truly pharmacologic effects of a drug used.

Its greatest value is its contribution to a more complete knowledge of the significance of blood pressure levels in an individual patient.

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DON'T SHOUT! — I CAN HEAR!

HAROLD F. SCHUKNECHT, M.D.*

A natural reaction in speaking to a deaf person is to raise the intensity of the voice. For many deafened persons these louder voice signals become intelligible because now they are capable of activating the excitatory mechanisms of the ear. There are some deafened persons, however, such as the aged, in whom intelligibility often is not improved by shouting. If one shouts at them they are apt to say, "Don't shout, I can hear." In fact, many aged people tell us that they can understand better if we do not speak so loudly. Another disturbing phenomenon is that grandpa occasionally can understand what is said behind his back so that the family suspicions are aroused to the point of accusing him of hearing only that which he desires to hear.

Eventually the family decides grandpa needs a hearing aid. The dealer in hearing aids is quite aware of the problems involved in fitting the aged person and, after a few tests, may even advise against its purchase. Nevertheless, grandpa's family, interested in his welfare, will see to it that he goes home with a hearing aid. Eventually, after several weeks trial, he gives up and puts it in the common burial ground for hearing aids, the bureau drawer. About this time grandpa is accused of being senile and uncooperative. He didn't refuse glasses when he needed them nor a crutch after he broke his hip. Why, then, won't he wear his hearing aid?

Old Age: Let us examine the clinical and pathological findings in the deafness of aging for an explanation of grandpa's uncooperative attitude. We find that there are two types of presbycusis. The first begins about the third decade of life, and is characterized by a progressive limitation of hearing for high frequencies. This high frequency hearing loss progresses so slowly over the years that usually it is imperceptible to the patient. The upper frequency limit for ordinary conversational speech is about 5000 cps and usually it is late in life before the process has involved these higher speech frequencies.

In a series of 72 cats, on whom my associates and I have performed hearing tests by the conditioned response method, we have found 5 animals with high tone deafness. A study of these animal ears and the ears of humans with high tone deafness revealed the pathological changes to consist of degeneration of the membranous labyrinth, beginning in the basal turn of the cochlea and proceeding toward the apex. This type of pathological change I have termed the "epithelial atrophy" type of presbycusis. It appears to be the otological manifestation of an aging process which affects all tissues, a close corollary existing in the skin where the changes are so characteristic that they are used as a yardstick to measure the age of the individual.

The second type of presbycusis I have termed "neural atrophy" because it is due to a decrease in population of neurons of the auditory pathways and is characterized by a discrimination loss out of proportion to the threshold loss for pure tones.

Ordinarily its onset is in older age and is superimposed upon the epithelial atrophy already described. The pathological features were characteristic in the ear of a 70 year old man on whom we acquired a hearing test immediately prior to death. The ear had the typical epithelial atrophic change involving the basal 3.3 mm. of the cochlea,

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but in addition there was a 30% to 50% loss of spiral ganglion cells extending from the 3.3 mm. to the 14.2 mm. region without accompanying changes in the organ of Corti or other structures of the membranous labyrinth. This loss of spiral ganglion cells appears to be related to a diffuse degenerative change involving the central nervous system. For example, it is well established that the aging brain suffers from a loss of nerve cells. The process seems to develop independently of cerebral arteriosclerosis but may co-exist with varying degrees of it. The clinical manifestation of loss of cortical neurons is senile dementia characterized by a gradual diminution of physical and mental capacity, an exaggeration of prior personality traits, increasing intellectual failure, impairment of memory, errors of judgement and insomnia. The cell outlines of the cortical neurons become shrunken and irregular, the cytoplasm becomes hyperchromatic, the Nissl material decreases, the nuclei become basophilic, and later there is glial proliferation and enuronophagia. A decrease in neuron population of the auditory pathways would be expected to have a negative effect on the amount of information which can be transmitted by these pathways.

In recent years ideas on communication and concepts of information transmission have been expressed in precise mathematical terms. Although few of us are interested or capable of understanding the mathematics involved in communication theory we readily appreciate its importance for speech intelligibility. The ear analyzes speech by recoding the sound signals into nerve impulses which travel up the auditory nerve. We know that the fundamental coding method is very simple in that a nerve impulse is either present or absent. This principle of "all or none" is basic to neurophysiology. Another limitation is that a single nerve fibre will carry a maximum of only about 800 to 1000 impulses per second. We may enumerate the variables in a neural pattern as follows: 1) frequency of impulses in a single fibre (below 1000 cps), 2) time relations between impulses in various fibres, 3) selectivity as to which fibres are being activated, and 4) the number of fibres activated. In spite of the "all or none" law the auditory pathways can carry all the information required for intelligibility of the spoken voice. This is possible because of the tremendous number of channels in this communication system, for we know there are about 35,000 fibres (or channels) in the human auditory nerve. In the pathological ear with a loss of nerve fibres a limitation is imposed on the coding mechanism and the amount of information which can be transmitted from the ear to the brain is less than normal.

Nerve Tumor: If a disproportionately severe discrimination loss is characteristic of neural lesions then it should also exist in patients with tumors involving the auditory nerve. Indeed, such is the case, for I have observed two patients with surgically and histologically proven acoustic neurinoma who manifested this same peculiar ability to hear but inability to understand in the involved ear. Mrs. W. had normal pure tone thresholds for speech frequencies and a speech discrimination score of 16%; whereas, Mrs. C. had a pure tone average in the speech range of 40 db and a discrimination score of zero. Of course, not all patients with acoustic neurinoma have these characteristic auditory findings for many are totally deaf in the involved ear at the time of the first examination. Then there are also those in whom the auditory findings are suggestive of combined neural and cochlear degeneration. In these cases the discrimination scores are somewhat better comparatively and there is partial loudness recruitment. The most likely explanation for the cochlear damage is that the tumor has compromised the circulation by choking the internal auditory artery.

Experimental Nerve Section: Thus far we have not been able to devise a method for determining an animal's ability to discriminate complicated auditory signals. We do have accurate methods, however, for determining pure tone thresholds for animals, so an experiment was designed whereby we could test the concept that the nerve fibre population can be reduced without creating a pure tone threshold loss. Accordingly partial section of the cochlear nerve was performed on twelve cats on which hearing tests were performed and a correlative study made of threshold losses and nerve fibre population. The procedure for each animal was as follows: The function of one ear was destroyed by a sterile surgical procedure. The animal was then trained to respond to pure tone auditory stimuli by moving forward in a rotating cage to avoid shock. Audiograms were made, using this conditioned response as an indicator of hearing. After base line audiograms had been obtained for each animal a surgical procedure was performed to section partially the cochlear nerve. By an approach through the posterior cranial fossa a portion of the cerebellar hemisphere was removed so as to expose the superior surface of the petrous portion of the temporal bone. With small dental burs the bone was removed in an oval area antero-medial to the arcuate eminence and immediately superior to the internal auditory canal. The facial nerve and the superior division of the vestibular nerve were exposed to view. By retracting the facial nerve anteriorly and the superior division of the vestibular nerve posteriorly, it was possible to expose the cochlear nerve as it entered the modiolus. The cochlear nerve was partially sectioned by gently moving a needle through a selected portion of the nerve trunk. Several weeks later audiograms were made, following which the animals were sacrificed by arterial perfusion with Heidenhain-Susa solution. The cochleae were graphically reconstructed from serial sections, and counts were made of the hair cell and spiral ganglion cell populations. The cell counts of several cochleae revealed that up to 75% of nerve fibres had been destroyed without creating threshold elevations for frequencies having their fields of excitation in those regions. Loss of more than 75% of the nerve fibres did create threshold elevations; or, in other words, the findings of this experiment means that for pure tone stimuli an impulse of threshold magnitude can be conducted when only 25% of the nerve fibres remain.

Conclusions: We may consider the spiral ganglion and its nerve fibres to be a part of a complicated communication system consisting in the human of about 35,000 channels. Among the variables which determine the amount of information which can be coded and transmitted over this system is the number of functioning channels or, in this case, nerve fibres. A deficiency in the number of auditory nerve fibres results in a system which can transmit simple signals of threshold magnitude, but cannot handle the complex signals of speech.

In grandpa's ear the neural patterns for speech are markedly distorted and sound garbled to him. To amplify the speech signal reaching his ear creates only a louder garbled signal and does not clarify it. He, therefore, may find a hearing aid to be of no use to him. A distorted speech pattern sometimes is more intelligible at moderate intensities than at high intensities and, therefore, grandpa may hear what he is not supposed to hear.

Putting it briefly and to the point, grandpa's ear is working fairly well, but his communication system is defective. Therefore, he may reprimand you in defiant tones "Don't shout! I can hear!"

MYOFASCIAL PAIN SYNDROMES

Part I — General Characteristics and Treatment

CHARLES LONG, II, M.D.*

"The phenomena of pain belong to that borderland between the body and the soul about which it is so delightful to speculate from the comfort of an armchair, but which offers such formidable obstacles to scientific inquiry."

With these words Kellgren[1] opens his excellent discussion of "Deep Pain Sensibility" and it is with similar caution that the entire subject of "Myofascial Pain Syndromes" must be approached. No attempt will be made to explain the pathologic origins of the syndromes which will be discussed in this paper. Under the name of fibrositis, extra-articular rheumatism, and numerous eponymic syndromes the etiology of the myofascial pain syndromes has been attached[2] in turn to trauma, infection (focal or otherwise), fatigue, vascular, metabolic, postural, occupational and psychogenic factors. It is most likely that any or all of these factors may be operative and an intelligent approach must take all possibilities into account. Apparently we are dealing with a pattern of non-specific shock organ response to stress.[3]

One of the only certain facts about these syndromes is the fact that they exist. Every attempt to trace them as pathological entities has proven their elusiveness. There is at present no consistent evidence concerning the pathological changes occurring in the muscles, fascia, ligaments and periosteum which are the reputed seat of the disease. The theory of herniation of fat particles[6] and the theories of actual inflammation of fibrous tissue structures[7] break down under careful microscopic scrutiny which so far has turned up nothing constant.[2,4,5]

These syndromes all combine the existence of pain with the presence of tenderness in soft tissues. The pain may appear directly at the point of tenderness, or it may appear at a distant point of reference. If the pain is distant from the point of tenderness, it is customary to call the distant area the "target" area and the tender area the "trigger" area.[8] These are so named because pressure over the trigger area often reproduces pain in the target area—in addition to the immediate local tenderness. Infiltration of the trigger area with a local anesthetic abolishes the pain in the target area. If the patient's pain is located primarily at the major site of tenderness, local infiltration will relieve the pain.

The syndromes to be discussed are part of a single family of clinical entities with common characteristics, including the above trigger mechanisms and responses to local anesthetic infiltration. All members of the family have a similar type of pain. The pain is aching in nature, diffuse and hard to localize, sometimes actually migrating about on an extremity or on the trunk. It is aggravated by sudden changes in the weather, and especially by cool, damp weather. It is almost invariably made worse during times of emotional stress or tension. One of the most disagreeable characteristics of the pain is its accompaniment by the "gelling" phenomenon. This phenomenon is typified by stiffness of joints in the involved area after moderate periods of inactivity. The stiffness-pain combination is relieved by movement of the affected segments.

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Although trigger points may exist apparently within any mesodermal tissue between the bones and the skin,[3] the syndromes mentioned here are assumed to have their trigger areas primarily within muscle tissue. Therefore in addition to pain and stiffness after inactivity, the patient often also has pain after prolonged activity, due to stimulation of the trigger point within the muscle. The patient therefore gives a history of stiffness at rest, aching pain after long resting (with a necessity for frequent shifts in position), followed by relief of pain on first moving about, followed in turn by a gradual return of severe aching pain and tiredness after moderate amounts of activity.

The myofascial pain syndromes may be acute, subacute, or chronic. In any phase they are differentiated from other forms of rheumatic disease and from neurologic disorders by the above typical findings and symptoms, plus the absence of significant changes in vital signs, sedimentation rate, circulating white cells, muscle strength (except as restricted by pain), and deep tendon reflexes. Hyperalgesia of the skin to pinprick over the reference or target area is not uncommon, especially in the acute stage.

The acute stage is characterized by the onset over a period of hours or days of the above-described severe, aching pain, accompanied by an increase in pain on motion. In both the trigger area and the reference area there is muscle spasm,[9] a combination of severe tenderness and tightness of the palpated areas. There is often a persistence of skin blanching, simulating dermatographia, plus a tendency to flaring as encountered in histamine injection.[3] In the acute stage the patient will not tolerate much palpation, and such examination should be kept at a minimum to prevent the development of further spasm and pain. This can be referred to as a "hot" muscle or trigger area, and the further evolution can be considered a cooling off of the process.

The primary weapon in treatment of the acute stage of myofascitis (if such we must call it) is reflex blockade—intense heat, directed at both the trigger and reference areas—or intense cold directed at these areas. Some authors even advocate the alternate use of these modalities. Moist heat seems empirically more effective than dry heat, so that hot packs and various forms of steam applications are most often used. Ethylchloride spray serves as a method of applying intense cold; this is a method of unusual effectiveness,[8] considering its extreme simplicity. Each of these reflex blockade methods is assumed to act by "jamming the frequency" on which the trigger point is broadcasting in the spinal cord. The cord level of trigger and target are usually within a few vertebral segments of each other; the intense afferent bombardment from the heat or cold apparently blocks the deep pain for sufficient time to upset the primary cycle of pain-spasm-pain.*

The concomitant use of anodynes in the acute stage is usually necessary. Aspirin will often suffice in large doses, but codeine is necessary in some cases, each combined with barbiturates in anxious persons. The presence of major psychogenic factors in the etiology and continuation of these syndromes has been mentioned. The patient gains a fair amount of his relief from the reassurance by the physician that there is "nothing serious" wrong and that he does "not have arthritis." It is certainly not

*Diathermy is empirically noted often to increase pain in early fibrositis and should not be used in acute cases.

necessary to x-ray every case of acute myofascitis, but any failure to respond in a reasonable period of time (two or three days) should prompt a vigorous diagnostic search, including appropriate x-rays. The relative lack of ultimate severity of the syndrome should not mitigate against hospitalization during the acute phase if the patient is extremely uncomfortable. Close following and dogged changing of therapy in the absence of response is one of the major keys to success in treatment of myofascitis; such a program sometimes necessitates hospitalization in any phase of the disease.

The subacute stage is entered as the extreme tenderness of the involved area cools off. In this stage the pain has subsided to a dull, but fairly constant ache and one of the major problems may be lack of sleep because of inability to get comfortable. It is in this phase that injection therapy becomes valuable. Although injection is often helpful in acute cases of back or neck sprain, it seems more irritating than useful in acute fibrositis. It is therefore reserved for use when the myofascitis (recognized clinically by tenderness) has become localized to one or a few easily accessible spots. During the subacute stage ethyl chloride spray is still a very useful agent, and of course salicylates form a foundation of the total program. This author has not used the steroids or Butazolidin in the acute stage, but has preferred to reserve their use for more refractory cases which do not respond in the subacute or chronic stages. Both of these drugs are used in combination with physical treatment methods, and their administration is continued for as short a time as possible.

In the chronic stage of myofascitis we come to the controversial subject of the "fibrositic nodule." There exists little doubt in the minds of persons who continually are engaged in palpating muscles that nodules are present in the chronic phase of myofascial pain syndromes. The inability to demonstrate them microscopically does not prove their absence, since probably a major part of their pathophysiology is spasm. The fibrositic nodule forms at the corresponding trigger area for the given syndrome. Such a nodule is by no means always present, so that chronic trigger points can exist manifested only by tenderness and by severe pain on needling. The chronic fibrositic area when needled presents a characteristic feel as though the needle were being firmly grasped by the muscle; on some occasions a grittiness is felt during the needle passage (but nothing is found on x-ray to suggest calcium deposition!)

The treatment of the chronic trigger point or nodule is by a combination of intense surface heat, specific trigger point injection, massage and/or stretching. The heat can be applied at home by an infra-red bulb; fifteen minutes once a day will suffice. The trigger point injection can be made with any calibre needle and, mirabile dictu, can be partially effective even if a dry needling is performed. Saline injections alone will relieve a large percentage of cases; 1% procaine hydrochloride (10 cc) will relieve a still larger percentage. This injection is routinely followed in our clinic by 1 cc (25 mgm) of hydrocortisone suspension; the two agents are not mixed.

Stretching is carried out in a variety of common-sense fashions, each of which will be mentioned under the appropriate syndrome. Massage itself is indeed a form of stretching the involved area in chronic myofascitis. It is inferior in rapidity of effect to injection, but its effects are just as lasting. Because of the necessity to return for repeated, expert massage at the hands of the physical therapist the massage treatment usually becomes more expensive than injection alone. On occasion the two may

be combined, or they may be substituted one for the other in the event of treatment failure.

It is common for the patient to present himself to the physician with a history of chronic myofascitis existing many months or years. A careful history may show episodes dating from childhood and encompassing practically all of the various possible symptom combinations. Such patients are said to have a "fibrositic diathesis" or increased susceptibility of muscle as a shock organ to stress. Psychogenic factors rate high among the aggravating factors of fibrositis in such patients and the physician should not hesitate to use transference, re-assurance, and environmental manipulation in the relief of stress and tension in the patient's life.

Also, in the chronic fibrositic an occupational posture or repetitive motion factor may be operative, so that a job change will sometimes be indicated. If job change is impossible, different work habits should be encouraged. Certain postural excercises—usually stretching—may be helpful.

In the next issue of this journal will be discussed the following family of myofascial pain syndromes: Occipitofrontal tension headaches; trapezius syndrome; scapulocostal syndrome; scapulohumeral syndrome; anterior chest wall syndrome; abdominal wall syndrome; lumbago; pelvic floor syndrome; adductor longus syndrome; scalenus anticus syndrome.

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CONGENITAL ANOMALIES OF THE BRAIN AND SPINAL CORD

EDGAR A. KAHN, M.D.*

Congenital anomalies of the brain and spinal cord may arise as a result of hereditary factors or from disturbances in the intra-uterine environment of the embryo. The parents of a child with hydrocephalus, cranium bifidum, or myelomeningocele are naturally concerned as to whether subsequent children will be similarly affected, and often question the physician concerning this possibility.

From the study of Record and McKeown, there is little doubt that following the birth of a child with anencephalus, spina bifida, or hydrocephalus, there appears to be a significantly increased probability of recurrence amounting to about five times normal expectation. The expectation of the population at large of having a child with such a malformation is about one in two hundred. Therefore, in families who have had one child with anencephalus, spina bifida, or hydrocephalus it would be expected, from the statistics of Record and McKeown, that one child in the next forty born to such a family might have one of these abnormalities.

According to Doctor James V. Neel of the University of Michigan Heredity Clinic, the present data on man still do not indicate whether the increased risk of defects of the nervous system in subsequent children is the result of genetic or non-genetic factors. It must be remembered that children with defects of the nervous system are usually unable to propagate, thus further limiting any hereditary tendency from expressing itself. Furthermore, if a first child is affected with a congenital anomaly of the nervous system, parents may tend to have no other children, thus further preventing the hereditary factor from expressing itself.

HYDROCEPHALUS

Before discussing congenital hydrocephalus I should like to discuss five different ways in which ventricular dilatation can be produced:

1. By an overproduction of cerebro-spinal fluid. This is usually due to a papilloma of the chorid plexus and is the least common cause of hydrocephalus.
2. By obstruction to the outflow of cerebro-spinal fluid within the ventricular system or at the foramina of exit in the posterior fossa: The most common cause of ventricular obstruction is tumor. However, a membrane can close the aqueduct of Sylvius or stenosis of the aqueduct of Sylvius can result in a specific type of hydrocephalus, which usually manifests itself symptomatically just after puberty.
3. Hydrocephalus by obstruction in the communicating channels: By "communicating channels" are meant the subarachnoid conduits through which the cerebro-spinal fluid flows to reach the absorptive mechanism on the surface of the cerebral hemispheres.

   Closure of the communicating channels can be caused by a developmental disturbance or by any pre or postnatal infection which might produce an arachnoiditis. The communicating is the commonest type of congenital hydrocephalus but the exact mechanism is certainly not yet understood. In such cases dye placed in the lateral ventricles would be recovered promptly on lumbar puncture, whereas in the obstructive type of hydrocephalus the dye

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would not appear.

4. Hydrocephalus due to failure in development of, or obstruction in, the absorptive mechanism: It is almost impossible to differentiate this condition clinically from a communicating type of hydrocephalus. The treatment of the two conditions, however, would be the same.
5. Hydrocephalus due to increase in protein in cerebro-spinal fluid: Gardner has recently put forth the ingenious theory that an increase in protein in the cerebro-spinal fluid might delay its absorption sufficiently to produce an increase in intracranial pressure or hydrocephalus or both. He suggests that the papilledema somtimes found in spinal cord tumor, small acoustic neurinomas and the Guillan-Barre' syndromes may result from this cause. Additional evidence is needed to prove this theory, however.

TREATMENT OF CONGENITAL HYDROCEPHALUS

When a child with evidence of hydrocephalus enters the clinic, the routine study is usually as follows:

The ventricle is tapped and as clear spinal fluid flows from the needle, it is gradually withdrawn until the fluid ceases to flow. The needle is then grasped flush with the scalp and withdrawn. This gives a comparatively accurate idea of the thickness of the brain substance. If it is less than one centimeter, it is probably unwise to attempt any type of operative procedure. If the brain substance is more than one centimeter in thickness one to two ccs. of dye are placed in the ventricle. After fifteen minutes a lumbar puncture is performed. If the dye is obtained it means that obstruction is not present in the ventricular system or at the foramina of exit of the fourth ventricle. It still does not tell whether the defect is in the communicating channels or in the absorptive mechanism.

The operation of choice in the female is making a communication between the lumbar subarachnoid space and the fallopian tube after the method of Harsh. So far the results have been promising and the operation is physiological in that there is no loss of electrolytes.

The Matson procedure has been followed by a number of good results; however, because of loss of electrolytes there is some danger, particularly in hot weather. There is also the danger that in females particularly, an ascending infection may result in meningitis.

If obstructive hydrocephalus is believed present, air studies are carried out in an effort to demonstrate the location of the block. If this block cannot be relieved surgically a long tube may be placed connecting the lateral ventricle with the ureter, peritoneal cavity or fallopian tube. It is more common than not, however, that this long tube will obstruct, kink, or be drawn back up into the lateral ventricle. In our hands, the results in its use have been unsatisfactory.

Choroid plexectomy has been successful in some hands. An ideal operation for hydrocephalus of any type has not yet been produced.

DIFFERENTIAL DIAGNOSIS IN HYDROCEPHALUS

Congenital hydrocephalus may be simulated by a subdural hematoma. The shape of the head and the bulging of the fontanelle may be exactly the same in the two conditions. In a child with a subdural hematoma, which is not too long standing, however, the facial expression is, as a rule, much more intelligent than it is in the hydrocephalic infant. Subdural hematoma usually does not appear symptomatically before

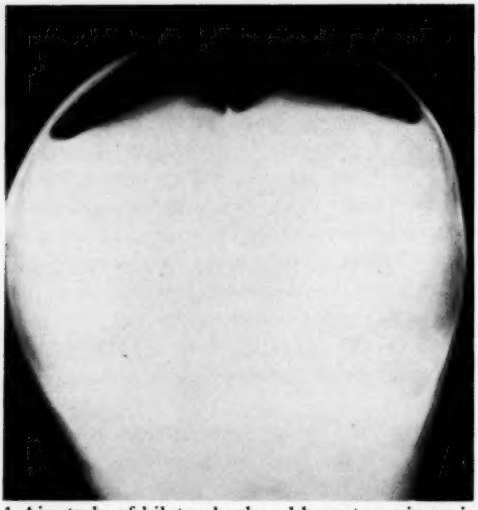

Fig. 1 Air study of bilateral subural hematoma in an infant.

the age of three months. Convulsions are common as are retinal hemorrhages in subdural hematoma, but rare in hydrocephalus. The diagnosis is made by subdural puncture.

Treatment of subdural hematoma is aspiration for a period of several weeks. If this is not effective osteoplastic craniotomy must be performed with partial removal of the membranes.

Fig. 2 Hydranencephaly. Arrow points to choroid plexus.

Another condition, which must be differentiated from hydrocephalus is hydranencephaly. This is a condition in which the infant may appear normal at birth. Within a week or so, however, it becomes obvious that he is retarded. The head may then enlarge. Transillumination reveals evidence of complete absence of the brain in the fronto-parietal area. The cause of hydranencephaly is probably congenital obstruction of the foramina of Monro.

CRANIUM BIFIDUM

The occurrence of cranium bifidum with encephalocele in proportion to surgically significant spina bifida is about 1:7. In comparison with spina bifida occulta, simple cranium bifidum is an extremely rare lesion. The patient with an encephalocele, particularly when it is occipital, is apt to have other anomalies of the brain such as microgyria, hydrocephalus, or brain stem deformities. In spite of this, Ingraham and Swan estimate that 34 percent of infants with encephalocele may expect a relatively normal life, following appropriate surgery.

The occipital encephaloceles are sometimes exceedingly complicated and carry the poorest prognosis. In one child, who died at operation when an abnormal circular sinus was opened, the brain stem at autopsy, was found to be rotated ninety degrees.

From a surgical point of view the most interesting of these lesions have been nasal encephaloceles. Two of these were identical, the tips of both frontal lobes having been contained in an unsightly sac, which presented itself at the root of the nose.

CRANIOSTENOSIS

Craniostenosis is a term used by Virchow to designate various types of skull deformity resulting from, or at least associated with, premature closure of the cranial sutures. It was Virchow's theory that when precocious synostosis of two cranial bones through ossification of the suture line is encountered, the growth of these bones

Fig. 3 Oxycephalic type of craniostenosis (10 days postoperative).

perpendicular to the suture line is hindered while overgrowth takes place elsewhere. Thus with closure of the coronal sutures, growth in an anteroposterior direction is inhibited while lateral overgrowth is stimulated and a brachycephalic type of craniostenosis results. Likewise, if the sagittal suture closes prematurely, the skull becomes long and narrow, the dolichocephalic type occurring. If all of the sutures synostose prematurely but the anterior fontanelle remains open for a period of time the oxycephalic or "tower" skull results. Cruzon's disease is an unsightly type of craniostenosis in which the child shows exophthalmos, a bird-like nose and a protruding lower jaw. This facial deformity results from premature synostosis of the facial bones as well as those of the skull.

Premature closure of several of the sutures may only result in ugly deformities of the skull. Craniostenosis, however, usually takes place before birth and, if sufficient sutures are involved, increased intracranial pressure will develop as the brain expands. In time, this results in mental deterioration and visual loss. The object of treatment is to allow expansion of the skull by surgical creation of new suture lines before irreparable damage has taken place. It is, therefore, imperative that the pediatrician recognize this condition early and refer the infant to a surgeon for treatment as soon as possible.

SPINA BIFIDA

Spina bifida is a term loosely used by physicians when they wish to refer to a saccular protrusion which usually contains nerve roots or spinal cord and its membranes. The herniation of nervous tissue through a vertebral defect should more correctly be described as a myelomeningocele, or if it consists only of spinal cord membranes it should be called a meningocele. Spina bifida may be classified as follows:

Spina bifida occulta in which there is a vertebral defect but no obvious protrusion. This common condition is found in about 25 percent of normal individuals. It almost always occurs in the sacral region, which is the last portion of the vertebral column to fuse.

Meningocele where is a protrusion of membranes of the spinal cord only, through the bifid vertebrae. The sac is usually covered by healthy skin but somtimes is formed by a transparent, parchment-like membrane. The base or neck of the sac may be broad but occasionally is narrowed down to a fine stalk. There is usually no neurological defect associated with a true meningocele. As a surgical curiosity, a meningocele may protrude anteriorly through a vertebral defect, simulating an abdominal tumor, or laterally into the chest through an intervertebral foramen. We have seen two cases of the latter in which the preoperative diagnosis has been neurofibroma.

Myelomeningocele where there is a protrusion of spinal cord or nerve roots covered at least by a membrane. This is a more common lesion than meningocele in a proportion of about 7:1. In more than half of the cases of myelomeningocele there is a severe neurologic defect such as paralytic club feet, relaxation of the sphincters, or hydrocephalus. The myelomeningocele occurs least commonly in the dorsal region, which, embryologically, is the first part of the vertebral canal to close.

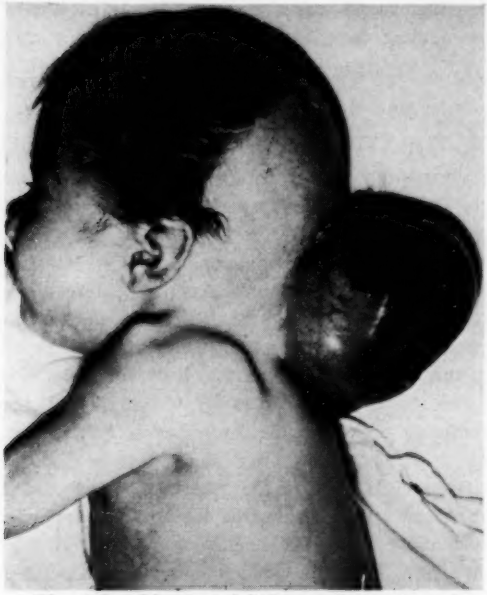

Fig. 4 Combined occipital encephalocele and cervical myelomeningocele.

Myeloschisis is the term applied to a condition represented by a wide open, weeping, shiny, reddish mass which has protruded entirely through the vertebral defect. This is the most marked of the developmental defects of the spinal cord.

Embryological studies carried out by Patten, in the Department of Anatomy at the University of Michigan indicate the extraordinarily early age at which this defect is established. The youngest of the embryos in his series which shows this defect was 8 mm. in crown-rump length, with a presumptive fertilization age of only a little more than five weeks. The traditional interpretation of such defects is based on the developmental arrest concept, but Patten's quantitative assessment of the neural plate tissue in the region of the defect seems to indicate—to the contrary—that local overgrowth of the neural plate is responsible. Myeloschisis is almost invariably fatal within a few months after birth.

SURGICAL TREATMENT

The purpose of operations upon myelomeningoceles is to free all nervous tissue from the tethering effect of the sac, returning the nerve roots and cord to the vertebral canal without increasing the neurological defect. This is often more easily said than done. Care must be taken not to transect functioning cord tissue which has attached itself to the sac and doubled back into the spinal canal. A nerve stimulator is of value here in determining what nervous tissue can be sacrificed. In spite of extreme care, however, the nervous defect is often increased by the operative procedure.

We like to wait as long as possible before operating upon most myelomeningoceles. This is so that hydrocephalus may not be precipitated by the procedure.

We never operated upon patients with paralysis of the legs or sphincters or with

impending hydrocephalus. Occasionally where a sac is extremely large, it may be removed to facilitate nursing care in spite of paralysis.

Where rupture of the sac appears eminent and paralysis is not present, operation must be performed as an emergency.

LIPOMAS OF THE CONUS MEDULLARIS AND CAUDA EQUINA

This particular congenital anomaly of the spinal cord has been recorded in the literature surprisingly seldom. The reason may be that a lipoma of the cord is often confused with the fatty mass which is commonly associated with a myelomeingocele. These lipomas of the cord represent a clinicopathological entity: From birth a non-fluctuant mass is present over the sacral area. Roentgenograms almost invariably show a bifid deformity of the sacrum and of the lower two lumbar laminae. Urinary incontinence or nocturnal enuresis may appear at any time. When exposed at operation the subcutaneous lipoma narrows to a stalk which traverses the bifid vertebra entering the dura though a sizable oval opening to merge with the conus medullaris and cauda equina. With the tethering action of the lipoma it is easy to see how neurological symptoms could arise with growth of the spine. Bassett published nine cases in 1950 from the University Hospital. He showed that where the spinal cord is fixed by a lipoma, the stalk of which penetrates the dura in the lumbosacral area, the nerve roots from the cord segment just above the point of fixation course upward to enter the intervetebral foramina. We have seen this same phenomenon associated with a congenital tumor of the filum terminale which was merged with the dura in the lower end of the dural sac.

CONGENITAL DERMAL SINUS

If in a child with meningitis, the causative organism is not the meningococcus and the source of infection is unknown, the midline of the back and occiput should be searched for evidence of a congenital dermal sinus. Likewise, if meningitis has recurred in the absence of obvious evidence of chronic infection close to the meninges, it is more than possible that the individual is harboring a congenital dermal sinus.

Walker and Bucy first used the term, "congenital dermal sinus," in 1934 and called attention to the fact that the chain of events—infection in a midline dermal sinus followed by meningitis and paralysis—constitutes a clinicopathological entity. They concluded that, at that time in embryological development (late in the first month of intrauterine life) when the cutaneous ectoderm and the neural ectoderm should have become separated, the cleavage between them was incomplete at the particular point where the sinus occurred. Thus the neural tube carried down with it a narrow invagination of skin, the connective tissue layer of which was continous with the connective tissue of the covering of the spinal cord, the meninges. Given such a developmental background, one can easily understand how meningitis can occur if the sinus should become infected.

Congenital dermal sinuses may lead to dermoid and epidermoid tumors of both the brain and the spinal cord. Dermoid and epidermoid tumors of the spinal cord, without a congenital dermal sinus, are not at all rare. Of the two the epidermoid cyst is more frequently encountered, however. Pain is conspicuously absent in dermoid and epidermoid tumors, probably because of the very gradual enlargement of the tumor, its soft smooth character, and its relatively complete fixation. Tumors of this

type may be very extensive. It is often impossible to remove the entire wall of the cyst without causing irreparable damage to the spinal cord or to the cauda equina. It is probable, moreover, that complete removal of the epithelial lining of the epidermoid cyst is necessary in order to prevent recurrence, just as it is with a sebaceous cyst. Sufficiently long periods of case observation have not as yet been recorded to establish this point. It is certain, however, that irreparable damage to the cord should be avoided during the first operation.

The midline dermoid and epidermoid tumors of the brain have been well described by Matson and Ingraham. Most of these tumors are connected to the surface by congenital dermal sinuses, exactly in the same manner as are those of the spinal cord, thus making it possible for infection to precipitate the first sign or symptom. All of the sebaceous material must be removed from these cysts in the uninfected case, and probably the wall as well, or an infective meningitis may develop on the basis of chemical irritation. The risk of this type of meningitis may not be as great as it was before the days of the antibiotics when Critchley and Ferguson reported three cases of incompletely excised cholesteatoma of the brain, all of whom succumbed to meningitis. The cholesteatoma of the brain are not so difficult to remove completely as are those of the spinal cord where so little trauma can have such devastating effect.

Considerable confusion exists between congenital dermal sinuses in the lumbosacral region and pilonidal sinuses and cysts. The former are present from birth and appear as midline dimples, usually surrounded by hair or angiomatous skin. According to Doctor Carl V. Weller, a pilonidal cyst is an acquired lesion. It is almost always found in the sacrococcygeal region and usually appears in young, hairy males. A pilonidal cyst is apparently a reaction to the mechanical implantation of the hair of the patient in and beneath the skin of the midline of the postanal region. A similar lesion has been found between the fingers of barbers where hair follicles are normally absent.

Treatment of Congenital Dermal Sinus: In our experience, the patient with a congenital dermal sinus communicating with the spinal meninges is invariably a child. He has entered the hospital with meningitis or has just recently recovered from it. Penicillin, streptomycin and aureomycin are usually started immediately. If the opening of the sinus tract is inflamed, wet dressing may be applied for short periods. When the acute infection has subsided the sinus tract should be completely excised after it has been well exposed through a carefully performed laminectomy.

DIASTEMATOMYELIA

Diastematomyelia is a cumbersome term which has been used for more than 50 years to describe a cleft in the spinal cord which splits the cord in two, each half surrounded by its own dura. "Diplomyelia" is often used as a synonym for diastematomyelia but, in my opinion, actually refers to a doubling of the spinal cord. The latter condition is rarely of surgical significance and is more common than diastematomyelia. Diplomyelia may exist in the absence of any symptoms.

Diastematomyelia is accompanied by a midline bony spicule which has arisen from the posterior surface of the body of a vertebra and has passed through and impaled the spinal cord or cauda equina. With the relatively greater growth of the spine, traction may later be produced on the spinal cord or on its nerve roots.

The symptoms of diastemotomyelia are usually manifested first in children shortly after they have learned to walk. The first symptom is, as a rule, that of a disturbance in gait. Such a disturbance may consist in unilateral or bilateral weakness of the lower extremities, or in an increasing spastic paralysis. Bladder disturbance or a trophic ulcer of one or more toes may then be noticed or, as a matter of fact, may be the first symptom to be observed.

Examination of the back may reveal a tuft of hair or a lipoma lying over what is revealed by x-ray examination to be a spina bifida. On careful examination of the anteroposterior view of the spine, an abnormal line of increased density may be noted in the middle of the spinal canal. This is usually found in the region of a bizarre spina bifida occulta and represents a bony abnormality which has grown backwards through the spinal cord and its meninges. So far as we know, this abnormal line of increased density was first pointed out by Hamby in a case from which he had removed the midline bony spicule. Neuhauser, and his associates, have since been able to make the diagnosis preoperatively in a number of cases in the Children's Hospital in Boston. Of 11 cases operated upon at that hospital by Matson, Woods, Campbell and Ingraham, the correct preoperative diagnosis was made in eight by X-ray studies. In some cases pantopaque studies were carried out and revealed that the dural sac had been divided into two halves at the point of the bony spicule.

The operation for diastematomyelia follows the same approach as that described

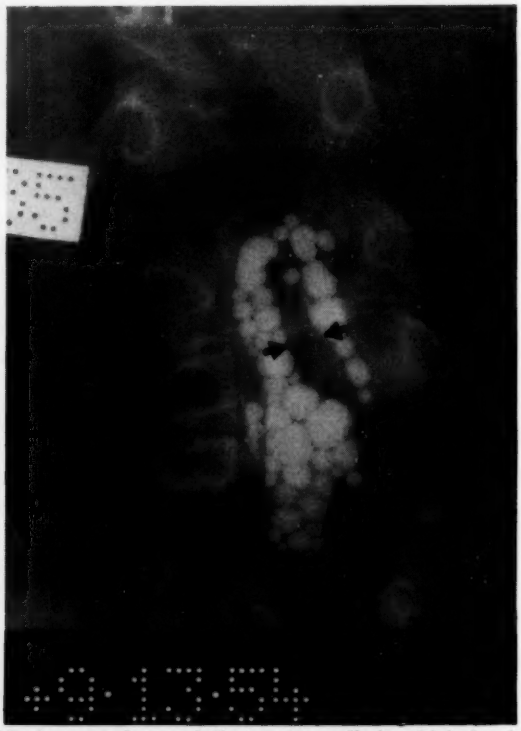

Fig. 5 Myelogram of case of diastematomyelia in which dural septum (arrows) was not excised at first operation.

for spina bifida occulta. When the bony spicule is encountered, it is dissected subperiosteally down to its attachment to the body of the vertebra from which it has arisen. We now believe that it is necessary to open the dura and obliterate the dural septum after the bony spicule has been removed. In one case where we failed to excise the septum, recurrence of symptoms took place five and a half years later. A myelogram (Fig. 5) was then performed and the typical midline defect of diastematomyelia was seen. At operation it noted that scar tissue had replaced the excised spicule of bone and was compressing the cord posteriorly as well. The scar-filled dural septum was excised and the dura closed posteriorly. Rapid improvement followed this procedure.

TERATOMAS OF THE SPINE

Although the teratoma of the sacrum is not specifically an anomaly of the nervous system, it is ordinarily treated by the neurosurgeon. The teratomas of the cervicodorsal and lumbar spine, however, are associated with a vertebral defect and sometimes with a meningocele or myelomeningocele.

The sacral teratoma, however, is a distinct entity. There is no connection with the meninges or spinal cord. It has invariably been associated, in our experience, with a defect on one side of the lower part of the sacrum and a total absence of the coccyx. In 20 such sacral teratomas which we have operated upon in this clinic only three were malignant.

Comment: These lesions may assume a tremendous size. Most observers in the past have concluded that sacral teratomas were in all instances vestiges of a reduced parasitic twin. More recently, however, Patten has pointed out another possible origin:

"The extraordinarily high incidence of trigerminal teratomata in precisely the region where the primitive streak of the embryo was formerly located may well mean that some of these masses originated by neoplastic growth of the tissue in this territory. In the embryo, the region of the primitive streak is a proliferation center from which cells entering all three of the germ layers are derived. It is quite logical, therefore, if it became involved in neoplastic growth that it would give rise to a teratomatous mass in which derivatives of all three of the germ layers were represented."

Patten is careful to emphasize that his interpretation in no way precludes the involvement of twinning in a certain portion of sacral teratomata. The possibility of an additional method of origin in this region, however, may well help explain the high incidence of teratomata in the sacral region as compared with other regions in which unequal conjoined twinning might be involved.

Surgical Treatment: If the teratoma is exceedingly large, necrosis may threaten, in which case the lesion must be excised immediately. The prognosis with teratomas is ordinarily excellent. We have experienced one recurrence of a benign teratoma where some of the tumor was inadvertently allowed to remain. It was successfully excised at a second operation.

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THE CLINICAL CARDIOVASCULAR FEATURES OF HYPERTHYROIDISM

F. Janney Smith, M.D.*

The fully developed clinical picture of toxic goiter or hyperthyroidism is familiar to all practitioners of medicine, consisting generally of weight loss, hyperthemia, nervousness, palpitation, tachycardia, struma, fine tremor of the extended fingers, prominence of the eyes and other eye signs, sweating, increased pulse pressure.

There are, however, a number of instances of toxic goiter where the presenting symptoms or complaints are such to be predominantly cardiac. This may lead to an impression, on the part of the patient, that his trouble is heart disease, and may indeed deceive the clinician as well, unless the latter carries a keen awareness of some of the vagaries of hyperthyroidism. These cases have thus come to be spoken of as "masked hyperthyroidism."

Among the cardiovascular features of hyperthyroidism, tachycardia is the most striking phenomenon encountered. The averaged pulse rate, in one hundred cases of hyperthyroidism, ranged around 120 per minute, although one individual in the series had a pulse rate of 44. The systolic blood pressure of patients with hyperthyroidism, in both the nodular and diffuse hyperplastic types, is often slightly elevated, and the diastolic pressure somewhat lowered; thus giving a pulse pressure equal to 50 percent or more of the systolic level. The pulse is dynamic in character, as a rule, and a collapsing or Corrigan pulse is frequently noted. Over the femoral artery, in the groin, a systolic tone is generally heard, occasionally of sufficient intensity to be characterized as a "pistol shot" sound. Inspection of the large arteries usually reveals well marked peripheral throbbing, especially notable in the abdominal aorta. The cardiac apex impulse is often diffuse, covering two or more interspaces, and in some cases abrupt, causing a distinct systolic shock. In others, there may be present a questionable thrill, difficult to time.

The character of the heart sounds may best be described as thudding or loud. The first sound at the apex is often abrupt and roughened, so that it has occasionally led examiners to speculate as to the possible presence of mitral stenosis.

Systolic murmurs are relatively common, usually present at the cardiac apex and louder in the pulmonic area. At times, the murmur in the pulmonic area may have a suggestively rubbing quality, and be increased in intensity by pressure with the bell of the stethoscope. This type of murmur generally disappears after relief of thyroid toxicity, while in a few who have subsequent relapses into hyperthyroidism, its presence may again be noted. It is interesting to speculate on the cause of this mumur. The strong probability exists that it may be related to the frequently observed dilatation of the pulmonary conus on x-ray in these individuals.

A slight degree of cardiac hypertrophy is present in about 40 percent of cases. In some individuals, on account of the rather violent apical pulsation communicated to the chest wall, an impression of cardiac hypertrophy, which may be present on

*Consultant, Division of Cardiology—Reprinted with permission from The Heart Bulletin, Nov.—Dec., 1955.

physical examination, fails confirmation on radiographic study.

Congestive cardiac failure is very rarely found in patients with hyperthyroidism who have regular cardiac rhythm, unless there is an associated valvular lesion or some degree of degenerative myocardial change from other cause than hyperthyroidism.

No single sign or manifestation should be thought pathognomonic of hyperthyroidism, but a combination of suggestive cardiovascular findings may be of considerable value in arriving at a correct diagnosis. The immediate effect of this condition on the heart is to produce a marked degree of cardiac over-activity, of which the various findings noted above are signals. This over-activity is generally commensurate in degree with the intensity of the thyroid toxicity and the increased cardiac output. Together with the other evidences of over-activity mentioned, we would like to stress as of suggestive value when present, the rubbing sound which we have described over the pulmonic area during systole, especially since it seems to have been largely overlooked in descriptions by other authors. This sound is of assistance to the diagnostician only in adding to the total sum of objective data suggesting hyperthyroidism. It may no doubt very occasionally be present in the absence of thyroid toxicity, but its intensity during the height of the disease, disappearance following relief of toxicity and reappearance in the few instances of recurrent hyperthyroidism has been striking.

The possibility of erroneously diagnosing rheumatic heart disease in cases of pure hyperthyoridism seldom offers real difficulty. The patients having mitral stenosis and hyperthyroidism generally have very frank signs of the former, with a pronounced presystolic rumbling murmur—a murmur which because of cardiac over-activity, is exaggerated during the period of thyroid intoxication. The examiner should not be too easily misled by less definite suggestions, such as a systolic shock or any ill-defined thrill palpated at the cardiac apex. Again, the peripheral arterial phenomena, which are common in aortic incompetence and occur in the majority of instances of hyperthyroidism (increased pulse pressure, Corrigan pulse, throbbing arteries and pistol shot sounds over the femoral artery) should merely serve to stimulate the examiner to consider the diagnosis of hyperthyroidism, especially if tachycardia be present and the diastolic murmur of aortic incompetence absent.

Electrocardiographic findings in hyperthyroid patients with sinus rhythm, are not diagnostic of this condition. However, it is frequently true that these patients show large P waves in lead II, above 1.7 mms., R waves above 16.5 mms., and tachycardia, and about 75 percent of them will show fine vibrations in the string shadow, reflecting the fine tremor of the extremities. The T waves are flat, diphasic or inverted in 25 percent of such patients. In electrocardiograms taken after relief of thyroid toxicity, there is a noticeable tendency for the P and R waves to decrease in voltage, the tremor to lessen and formerly flat or negative T waves to become again positive.

The following is a case report of an individual who presented himself to the examiner for what he believed to be a cardiac condition, where the diagnosis was proved to be hyperthyroidism. R. G., age 24, was a newspaper reporter. Two weeks previously, a life insurance examiner had noted the presence of a systolic murmur and questioned his insurability on this account. There had been no previous rheumatic history. The patient himself had no other complaints. He felt entirely well. On examination, there was a slight smooth enlargement of the thyroid. His blood pressure was 140/52, pulse

80/minute and regular. There was no evidence of cardiac hypertrophy. The rhythm was regular, but a systolic murmur, grade III, was heard in the pulmonic area. The intensity of this murmur, almost of a rubbing quality, increased with pressure of the bell of the stethoscope. It was somewhat less marked with the patient sitting. No diastolic murmur could be heard in the lateral position or after exercise. The pulse had a bounding quality. There was a slight tremor of the extended fingers and the eyes showed a slight lid-lag. The impression of a mild hyperthyroidism was confirmed by a basal metabolism determination of plus 32 percent. The patient was placed on Methimazole, and in three months time the basal metabolism dropped to plus 5 percent. The systolic murmur could scarely be heard, and it had lost its rubbing quality. The patient had gained eight pounds, the pulse rate had dropped to 68, blood pressure 128/70. He was presumed again to be euthyroid, and incidentally, to be insurable from a cardiac standpoint.

A second patient illustrative of "masked hyperthyroidism," was C. S., a female aged 69, seen in February, 1954. This patient had been treated elsewhere and the true nature of her illness had not been recognized. When first seen at the office, the predominating signs and symptoms were of a cardiac nature. She had had a thyroidectomy in 1910 for "inward goiter." A bilateral salpingoophorectomy had been done 4 years previously for a granulosa tumor of the right ovary. Her height was 5 feet, 3 inches, weight 239 pounds. Previously, in 1940, the weight had been 300 pounds. Her chief complaint was nausea and vomiting. She had diabetes and a blood sugar of 220. The blood pressure was 180/80. There was a pulse of 120. Paroxysms of auricular fibrillation were present. There was slight exophthalmos and lid-lag. Moist rales were noted at both bases, plus engorgement of the liver and ankle edema. The thyroid, beneath the scar, was increased in mass about two and a half times normal. Electrocardiogram showed sinus tachycardia, large P waves in lead II, diphasic T waves in leads I and II, flat T in AVL. A fine tremor was noted in the limb leads. X-rays showed moderate cardiac hypertrophy and some widening of the superior mediastinum. Tracer studies with I^{131} showed a high contact count in the mid line, an inch below the thyroid scar and a 24 hour retention of 70 percent. Methimazole, 10 mgms. every 6 hours was given initially. Two therapeutic doses of I^{131} orally, 5-29-54 and 9-27-54, resulted in complete clearing of the congestive failure and remission of the evidence of hyperthyroidism as well as clearing of the diabetic problem. The weight dropped to 214 pounds. The pulse was 80, blood pressure 170/90. However, the exophthalmos had progressively increased in the face of adequate control of the hyperthyroid state.

Patients with thyrotoxicosis seldom develop congestive failure unless their hearts are afflicted with an added handicap, such as rheumatic valvular disease or a degree of myocardial degenerative change which may occur with arteriosclerosis or hypertension. The majority of these patients are beyond 50. Usually the gland is of the nodular or adenomatous type and frequently auricular fibrillation developes, either in a transient manner or as an established arrhythmia. Characteristically, the ventricular rate may not slow on digitalization to the usual degree brought about by digitalis administration in euthyroid patients. In some of these patients, because of a low position of the thyroid, recognition of a small nodular goiter may be missed if the thyroid is only felt for in the recumbent position. In fact, the gland may be placed retrosternally, and

so escape physical detection all together. Such patients with congestive failure, where the thyroid element in the sum of clinical manifestations is overshadowed by the cardiac features, again constitute a large percentage of the group of "masked hyperthyroidism."

After relief of toxicity from hyperthyroidism, any cardiac insufficiency that remains must be thought to be due to other factors and treated accordingly.

In summary, it should be emphasized that a really careful use of the physician's own powers of observation, coupled with an awareness of the clinical cardiac manifestations encountered in hyperthyroidism, continues to be of inestimable value in the early detection of this condition.

PRELIMINARY EXPERIENCE WITH THE GLUTAMIC OXALOACETIC TRANSAMINASE DETERMINATION IN ACUTE MYOCARDIAL INFARCTION IN HUMANS

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DAN H. BASINSKI, Ph.D.** AND LAURIE DICKSON, M.D.***

Transaminase is an enzyme which catalyzes the tranfer of the amino group of a dicarboxylic amino acid to a keto acid to form a second amino acid and a second keto acid, thereby accomplishing the process of transamination. This reaction was first described by Braunstein and Kritzman in 1938. Since that time investigators have simplified the original and rather complex methods of assaying transaminase activity, and have established the presence of this activity in various tissues of the human body[1,2,3,4,5]. Glutamic-oxaloacetic transaminase, one of several different such enzymes, has been established as one of the most widely distributed, being found in decreasing concentration in the myocardium, liver, skeletal muscle and kidney. The advent of a reasonably practical method for assay of transaminase activity in human serum allows a more widespread utilization of this test as a clinical tool.

Use of this determination has recently been instituted here on a limited scale. This is a review of those reports appearing in current literature and leading to or supporting our decision to investigate the procedure, and a report of our preliminary findings. Assays were made on the serum of patients admitted for definite or suspected myocardial infarction either transmural or non-transmural. Two serial assays, 24 hours apart, were made. No attempt was made to follow the evolution of the reaction until increased activity returned to a normal level, except in two cases. Patients suspected of having co-existing destructive disease of the liver, skeletal muscle and/or kidney, conditions which may give rise to positive assays, were eliminated.

LaDue, Wroblewski and Karmen[5,6] have reported the only work done in humans in which a series of patients with myocardial infarction are included. After measuring transaminase activity in 50 normal individuals these investigators reported a normal range of 10 to 40 units. Activity in sera of 30 patients having incurred transmural infarctions yielded values of 100 to 6000 units on at least one occasion during the first five days following onset of the infarct. The sera of only 2 patients, of a total of 22 patients studied, with arteriosclerotic heart disease uncomplicated by myocardial infarction exhibited elevated levels of activity. This elevation was minimal. Increased activity could be obtained from sera of patients with destructive inflammatory lesions of the liver and kidney or lesions allowing tissue destruction due to sudden circulatory derangement in these organs. However, these yields were substantially below levels obtained in sera of patients with myocardial infarction.

To substantiate these findings this same group working alone and in conjunction with a second group[7,8] produced experimental infarcts in a total of 21 dogs. In 12

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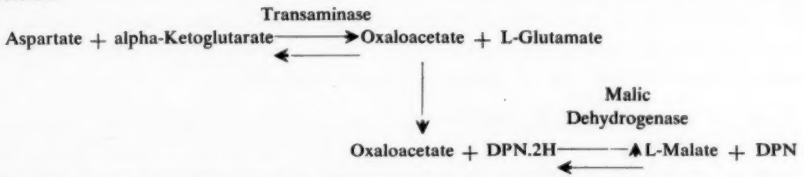
animals plastic microspheres were introduced into the coronary circulation resulting in coronary embolization and myocardial infarction. In the remaining 9, ligatures were placed about the coronary arteries and subsequently these arteries were closed after sufficient time had elapsed for the dogs to recover from effects of the anesthesia and thoracotomy. Since liver damage due to anesthesia or tissue destruction due to surgical procedure caused increased transaminase activity no ligations were done in the latter group until this activity had returned to normal and so remained for several days. In each instance of infarction a prompt and sustained elevation of transaminase activity was found. Following death portions of infarcted and healthy myocardium were removed. After homoginization of these sections transaminase activity was determined in each homoginate. Much less activity was consistently found in homoginates of infarcted myocardium than in homoginates of healthy myocardium.

The spectrophotometric method of Karmen, Wroblewski, and LaDue[6] was used for the assay of transaminase activity. The method has previously proven reliable by comparison of paired sera assay using the quantitative paper chromatographic technique. Assay of activity is predicated upon the measurement of the rate of oxydation of DPN.2H to DPN+ by oxyaloacetate, obtained during the transamination of aspartate and alpha-ketoglutarate (see Figure 1). The rate may be followed at wave length 340 mu in the model DU Beckman spectrophotometer. One unit of glutamic-oxaloacetic transaminase activity represents a decrease in optical density of 0.001/cc of serum/minute when measured at this wave length under specified conditions.

FIGURE 1

Reactions Utilized in the Assay of Glutamic Oxaloacetic Transaminase by the Spectrophotometric Method.



One unit of Glutamic Oxaloacetic Transaminase Activity represents a decrease in optical density of 0.001/cc of serum/minute when measured at wave length 340 mu at room temperature.

TABLE 1

Maximal Glutamic-Oxaloacetic Transaminase Activity in Nine Patients With Proven Myocardial Infarction.

Patient Number	Units of Activity
1	55 F
2	55 F
3	136 R
4	73 F
5	94 F
6	720 R
7	62
8	50 R
9	54 R

Capital letters following units of activity indicate whether this reaction fell below or above the preceding reaction.

Assays on three normal sera here have yielded values of 8 units, 14 units and 38 units. Twelve patients admitted to the cardiology service with proven or suspected infarcts have had serum transaminase assays on a minimum of two specimens. Nine patients had at least one serum yielding elevated activity, more than 40 units, (Table 1) each patient having EKG evidence of acute infarction. Three patients exhibited normal assays. Two of these did not have infarctions and the third incurred the infarction 10 days previous to admission.

One patient with a transmural posterior infarct had serial determination daily for 3 days. The first assay yielded 290 units, the second 580 units and the third 720 units. Death occurred during the night of the 3rd day.

One patient with a non-transmural anteroseptal infarction had serial determinations, done daily on each of 5 days. Units of activity in order were 12, 50, 32, 20 and 28.

It would seem that we may conclude from review of existing reports and our preliminary experience that: (1) the spectrophotometric assay of glutamic-oxaloacetic transaminase is a reasonably practical and reliable laboratory procedure. (2) increased activity may be found in sera of patients having incurred either transmural or non-transmural myocardial infarction. (3) increase in activity may be found within a short time after the occurrence of the infarct and may be sustained for a period of a few days or may return promptly to normal. (4) that cellular destruction in the liver or kidney gives rise to increased transaminase activity. (5) further utilization of the test is warranted.

It would seem reasonable to suspect that the degree of increase of transaminase activity is related to the amount of tissue damaged, but it probably is premature to declare that degree of damage may be estimated from the amount of elevation found.

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THE HENRY FORD HOSPITAL MEDICAL SOCIETY

PROGRAM FOR 1956

January 17, 1956—Tuesday, 8:15 p.m. — Henry Ford Hospital Auditorium

Preventive Surgery: Gains Versus Losses

Jonathan E. Rhoads, M.D., *Professor of Surgery,*

University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania

February 14, 1956—Tuesday, 8:15 p.m.—Henry Ford Hospital Auditorium

Diagnosis and Treatment of Disseminated Miliary Diseases of the Lungs

Marion A. Blankenhorn, M.D., *Professor of Medicine,*

University of Cincinnati College of Medicine, Cincinnati, Ohio

March 13, 1956—Tuesday, 8:15 p.m.—Henry Ford Hospital Auditorium

Investigation on pain.

Henry K. Beecher, M.D., *Dorr Professor of Research in Anesthesia,*

Harvard Medical School, Boston, Massachusetts

April, 1956—Date to be announced later—Henry Ford Hospital Auditorium

The Roy D. McClure Memorial Lecture

Evarts A. Graham, M.D., *Professor of Surgery,*

Washington University School of Medicine, St. Louis, Missouri

June 19, 1956—Tuesday, 8:15 p.m.—Henry Ford Hospital Auditorium

Subject to be announced

A. McGehee Harvey, M.D., *Professor of Medicine,*

The Johns Hopkins University School of Medicine, Baltimore, Maryland

ABSTRACTS OF RECENT PUBLICATIONS OF THE PROFESSIONAL STAFF OF THE HENRY FORD HOSPITAL AND THE EDSEL B. FORD INSTITUTE FOR MEDICAL RESEARCH

GASTRIC LIPOMA WITH HEMORRHAGE AND MYOCARDIAL ISCHEMIA SIMULATING MYOCARDIAL INFARCTION. W. L. AGEY AND J. L. PONKA. Gastroenterology 28:295, 1955.

Submucous gastric lipoma was first reported in 1835. In 1941 there were reviewed 34 cases, of which 17 were found at necropsy and 17 at operation. Subsequently, additional cases have been reported bringing the total number to 57. This is the 58th case and is the fourth case presenting gastrointestinal bleeding. The severe blood loss in this case accounted for the myocardial ischemia which in turn was evidently responsible for the clinical picture of myocardial infarction and the transient ECG changes. Medical management with replacement of blood and the use of an ulcer regimen until an exact diagnosis could be obtained resulted in healing of the mucosal ulceration. Roentgenological findings provided the impression that the lesion was benign. Gastroscopy was contemplated but rejected due to the possibility of a myocardial infarction, an absolute contraindication to gastroscopy. Surgery established the exact diagnosis. Massive gastrointestinal hemorrhage due to benign lipoma of the stomach is rare, four cases having been reported to date in the literature. Medical management, roentgen evaluation, and surgical intervention resulted in a cure.

*X-RAY DIFFRACTION POWDER DATA FOR STEROIDS. W. T. BEHER, J. PARSONS AND G. D. BAKER. Anal. Chem. 27:1569, 1955.

X-ray diffraction powder data and pattern photographs were presented for 39 steroids. The relative intensities and the distribution of lines in the patterns are useful for the identification of pure steroids.

INTENSIVE INSULIN SHOCK THERAPY; A FIVE-YEAR SURVEY. EARL P. BRANNON AND WALTER L. GRAHAM. Am. J. Psychiat. 111:659, 1955.

From April 15, 1948 to April 15, 1953, 615 patients were accepted for deep insulin shock therapy on the insulin therapy service of the Veterans Administration Hospital at Perry Point, Maryland; 528 patients completed a full course of treatment and were considered eligible for this survey. The method of treatment used was based upon the principles established by Shurley and Bond in the insulin unit of the Pennsylvania Hospital for Mental and Nervous Diseases, Philadelphia, Pennsylvania. Electric shock therapy was used in combination in those patients who did not have a satisfactory response from insulin alone. Analysis of the 528 patients treated revealed the following diagnoses: Paranoid schizophrenia, 247; catatonic schizophrenia, 138; hebephrenic schizophrenia, 21; simple schizophrenia, 12; schizophrenia, unclassified, 84; manic-depressive reaction, 16; miscellaneous reactions, 10. The social recovery rate ranged from 41.6 percent in the simple schizophrenias to 77.7 percent in the schizophrenias unclassified, and between 77.7 percent and 100 percent among the manic-depressive groups. It was found that the catatonic schizophrenias were the group with the highest percentage of relapse. Among the 528 patients were 513 males and 15 females. The social recovery rate between the two sexes was approximately equal.

*From Edsel B. Ford Institute for Medical Research.

One-hundred and thirty-eight negro patients were treated as compared to 390 white patients; the white group had a somewhat higher social recovery rate. The majority of patients treated, 62 percent, were within the 25 to 35 year age group. The group under 25 years had the best social recovery rate, and as the age increased the recovery rate was proportionally less. The series was studied for the effect of the duration of illness on the patient's chances of recovery. Reports of others on the decrease in rate of recovery proportional to length of illness were corroborated. It was, likewise, found that the length of hospitalization prior to institution of treatment materially decreased the recovery rate. An out-patient follow-up program for the socially recovered patients was developed. At the time of the survey of the 528 patients treated, 266 were still out of the hospital maintaining social recovery.

AN EVALUATION OF NEWER METHODS IN THE DIAGNOSIS OF HYPERPARATHYROIDISM. B. E. Brush, W. E. Chase, and M. A. Block. A.M.A. Arch. Surg. 71:342, 1955.

The diagnosis of primary hyperparathyroidism is difficult. The levels of serum calcium and phosphorus are the most important diagnostic tests, but these may be borderline or vary so much in a given individual that a definite diagnosis cannot be made. Two diagnostic tests have been introduced recently, based on the effect of the parathyroid hormone in decreasing renal reabsorption of inorganic phosphorus. Experience indicates that by the intravenous calcium tolerance test the diagnosis of hyperparathyroidism is suspected if the serum phosphorus fails to rise over 1 mg. per 100 cc. during the test and if the urinary excretion of phosphorus remains approximately the same as or is greater than the value obtained prior to the infusion of calcium. According to the phosphorus reabsorption test the renal reabsorption of phosphorus is over 90 percent in normal persons, whereas, it is considerably lower in patients with hyperparathyroidism. Our experience in utilizing the tests in four patients is reported. It appears likely that the tests will be of limited value in certain situations as in the differentiation of primary from secondary hyperparathyroidism but will not give a decisive answer in all suspected cases. However, the tests with further experience, may give a higher percentage of correct preoperative diagnoses.

CONTROLLED STUDIES IN THE TOPICAL APPLICATION OF HYDROCORTISONE IN VASOMOTOR RHINITIS. John H. Burger and Joseph H. Shaffer. Ann. New York Acad. Sci. 61:566, 1955.

One hundred patients with vasomotor rhinitis were selected from clinical allergy practice to participate in a "double blind technique" study of the local effect of hydrocortisone applied to the nasal mucous membranes. Two preparations in identical plastic spray bottles labeled Preparation A and Preparation B were used. One contained a buffered isotonic saline suspension of hydrocortisone acetate, 15 mg./ml., the other the buffered isotonic saline base without hydrocortisone. The contents were unknown to patient and investigator. Each patient served as his own control since he received both preparations during alternate periods of not less than one month. In tabulating results, the change in appearance of the nasal mucous membranes and the degree of symtomatic improvement were evaluted. Nasal smears were examined microscopically at monthly intervals, and the cellular elements of the exudate were recorded. Analysis of results showed subjective and/or objective improvement in 86 percent of the patients receiving the hydrocortisone preparation, while subjective benefit was obtained

by only 7 percent of patients receiving the placebo. No objective improvement occurred in this latter group. Furthermore, 14 percent of the patients receiving the placebo were worse compared with 2 percent of those using the hydrocortisone. Studies by the same method on 100 additional patients using a suspension of hydrocortisone acetate 5 mg./ml., of hydrocortisone free alcohol 5 mg./ml., and hydrocortisone free alcohol in solution 0.2 mg./ml., produced similar results. However, the free hydrocortisone solution was somewhat less effective than either concentration of the acetate suspension or the free hydrocortisone suspension. There was no evidence of systemic absorption or significant adverse effects with any of the four preparations, in the concentration used. No marked alteration of the nasal exudate, or change in histological appearance of polypi was noted after therapy. No lasting benefit was obtained from the use of any of the preparations. Symptoms returned in all patients 10 to 14 days after discontinuing therapy.

CARCINOMA OF THE PANCREAS: A REVIEW OF 160 CASES. CHARLES I. CERNEY AND ROBERT B. WALLACE. Am. Pract. 6:1370, 1955.

The average age was 57.9 years, and the male to female ratio was 2.7 to 1. Symptomatically, the cases could be divided into four groups, each of which could be accompanied or preceded by weight loss, change in bowel habit and, less often, diabetes. (1) Cases in which there is pain usually in the upper abdomen, sometimes in the lower often radiating to the back. It may be evanescent but usually returns, and may become progressive and severe. It is often worse at night, and aggravated by jarring. (2) Cases in which there is jaundice which may accompany pain as the first symptom. It is infrequently painless, is usually progressive but may be fluctuant for a time and eventually severe. It almost uniformly develops when the head of the pancreas is involved but may be present without this. (3) Cases in which the symptoms are the result of metastases, either in the lung, or erosions of metastases elsewhere in the abdomen. In these the primary lesion is usually unsuspected until revealed at surgery or autopsy. (4) Cases in which there are venous thrombi or migratory thrombophlebitis. This may be alone, but more often accompanies the other groups of symptoms, and occurs most often when the body and tail are involved. There are no positive physical findings early in the disease. The liver and an epigastric mass eventually become palpable. The gall bladder was frequently palpable and usually was large at surgery. No laboratory findings were diagnostic. The serum amylase and lipase were rarely helpful. Occult blood occurred in the stool of 32 percent. Gastrointestinal x-rays suggested the diagnosis in 23 percent of the cases. The average duration of the illness was 25 weeks.

THROMBOPHLEBITIS MIGRANS AND VISCERAL CARCINOMA. ROBERT H. DURHAM. A.M.A. Arch. Int. Med. 96:380, 1955.

An abstract embodying substantially this same material is published in this *Bulletin* 3:169, 1955.

*TEST OF A-NAPHTHYLAMINE-4, 8-DISULFONATE AGAINST A TRANSPLANTED DERMAL SARCOMA. ROBERT H. FOULKES. Cancer Res. Supp. No. 2, p. 53, 1955.

Sprague-Dawley albino rats with transplanted dibenzanthracene-induced dermal

*From Edsel B. Ford Institute for Medical Research.

tumors were employed. The tumors were 21-30 days post transplants. The compound in aqueous solution was injected subcutaneously twice weekly for 3 weeks at a dose of 50 mg./kg./injection. Observations on the tumors were made for 7 weeks after the last injection. Tumors were measured by the external largest and smallest axes. Noted were no retardation, no regression, no toxicity as judged by lack of weight loss, and no deaths in the 4 treated tumor-bearing animals compared with the controls. No histological changes were observed in the treated animals.

DIFFUSE LEPTOMENINGEAL CARCINOMATOSIS: Clinical And Pathologic Characteristics. GERALD O. GRAIN AND JEAN P. KARR. Neurology 5:706, 1955.

Invasion of the central nervous system by blood-borne metastatic foci is seen commonly in the brain parenchyma. A rapidly fatal result may occur with a purely subarachnoid and leptomeningeal invasion, apparently lymph-borne by way of peripheral perineural pathways. Two cases are reported in which autopsy revealed no blood-borne metastatic nodules in the brain substance, choroid plexus or meninges, making a total of 85 such cases now reported in the literature. Clinically, the condition resembles tuberculous meningitis without fever and with sterile fluid in which tumor cells may be found. Pathologically, the primary lesion is found most frequently in the stomach and the meningeal invasion occupies all parts of the subarachnoid spaces, infiltrating intradural portions of nerve roots and superficial cortical perivascular spaces. Evidence supporting a perineural invasion in these cases is presented. The survival and spread of the cancer cell in the subarachnoid space is related to the presence of glucose in the cerebrospinal fluid.

FOUR-YEAR STUDY CONCERNING THE INACTIVATION OF VIRUSES IN BLOOD AND PLASMA. FRANK W. HARTMAN, A. R. KELLY, AND G. A. LOGRIPPO. Gastroenterology 28:244, 1955.

Screening of 550 compounds for antiviral activity in plasma has revealed that most active viricides can be classified in one of seven groups, based on chemical structure. Of the active agents, nitrogen and sulfur mustard, ethylene oxide and beta-propiolactone (BPL) have shown the best potentialities for sterilizing blood or plasma. To date, beta-propiolactone appears the most promising of these compounds from a viricidal and toxicologic standpoint. The bulk of virus activity in plasma can be destroyed by relatively low concentrations of beta-propiolactone (1000 mg./1.), even in the case of the sturdiest laboratory virus. However, two to three times this basal concentration is required to inactivate residual traces of these viruses and to thus insure absence of infecting units in transfusion volumes of plasma. The extent to which the basal concentration must be augmented to overcome this so-called "trailing effect" appears to be a function of individual virus resistance. Therefore, the concentration required for complete sterilization of the serum hepatitis virus must necessarily be determined directly by human volunteer studies with that virus. Investigations of this type have been in progress elsewhere for some time. Such factors as virus titer and plasma protein concentration also influence the sterilizing dosage of this compound. Beta-propiolactone possesses possibilities for sterilizing erythrocyte suspensions. Beta-propiolactone and ultraviolet irradiation have been found to be mutually potentiating when used in combination for the sterilization of plasma. Plasma treated with beta-propiolactone displays a striking lack of toxicity even at concentrations three to four times those required for complete inactivation of laboratory viruses.

Over a 3-year period 241 patients have received 767 transfusions of plasma treated at viricidal concentrations without evidence of toxicity of production of serum hepatitis.

HYPOFIBRINOGENEMIA AND DEFECTS OF COAGULATION. C. PAUL HODGKINSON, JOHN H. LUZADRE, PAUL W. PIFER, LAYMOND A. SWINEHART, AND DONALD G. REMP. Obst. & Gynec. 5:465, 1955.

Using transient fibrinogen depression as observed in serial blood samples as a diagnostic "end point," the severity and incidence of thromboplastin influence on fibrinogen levels was evaluted in obstetric and gynecologic patients. It was possible to correlate relative fibrinogen values with incoagulable blood, blood clot stability, "obstetric shock," critical plasma fibrinogen level, and effectiveness of therapy. Pathologic defibrination results in massive precipitation of insoluble fibrin. The importance of massive embolization from intravascular coagulation as an important pathologic mechanism is gaining recognition. Obstetric shock and nonhemorrhagic traumatic shock are possibly on this basis. Organ insufficiency from fibrin embolization such as pituitary necrosis, bilateral renal cortical necrosis, and certain forms of cerebral thrombosis have been suggested as being associated with defibrination. The spectrum of effects resulting from lesser degrees of defibrination remains speculative. Hypofibrinogen reactions characteristic of defibrination have been identified with many types of tissue injury. Surgical trauma, absorption of the products of aseptic necrosis from intrauterine fetal autolysis, and uteroplacental trauma are well documented from serial fibrinogen studies. Excessive muscular activity has been suggested as a thromboplastin-provoking reaction. Convulsive eclampsia and unusually severe uterine contractions have been associated with fibrinogen depression. The observation that fibrin emboli and hemorrhage from defibrination have never been observed in nonconvulsive toxemia suggests the importance of abnormal muscular contraction as a defibrinating factor. Realization that the degree of surgical trauma may be directly related to the extent of defibrination is a sobering thought. One questions if flooding the circulatory system with insoluble fibrin during and immediately following a cutting operation may not serve as the nidus for subsequent phlebothrombosis and pulmonary embolism. These factors place a premium on atraumatic surgical procedures and especially upon atraumatic surgeons.

REHABILITATION IN ARTHRITIS: A Case Report. WILLIAM M. JACKSON, JOHN W. SIGLER, DWIGHT C. ENSIGN, JOSEPH L. FLEMING, AND CHARLES LONG. J. Michigan M. Soc. 54:330, 1955.

A patient disabled with arthritis is not only a candidate for organized therapy in a rehabilitation center but also should be the responsibility of every physician engaged in the practice of medicine. Most patients with arthritis are unusually grateful for any help they receive. The case presented represents one of "mixed arthritis," including elements of osteoarthritis, rheumatoid and traumatic types. The patient entered the hospital weighing 320 pounds and in bed from arthritic pain and weakness. After 215 days she left the hospital weighing 172 pounds and able to walk with crutches. Upon discharge she was still on crutches and had evidence of rheumatoid arthritis. Admitting the absence of curative therapy in most of the arthritides, there are available rehabilitative measures which can do much to relieve suffering, improve function, correct deformities and return the patient to a nearly normal, useful and hopeful life. These divide themselves into three general, overlapping categories. These

are the general medical care, the orthopedic measures which may be undertaken and the contributions of physical medicine.

*PROSTHETIC GROUP AND MECHANISM OF ACTION OF SUCCINIC DEHYDROGENASE. EDNA B. KEARNEY AND THOMAS P. SINGER. Resumes Des Communications Troisieme Congres International de Biochemie, Brussels, 1955, p. 55.

Homogeneous succinic dehydrogenase contains two atoms Fe per mole. From aged acetone powders an enzyme with one atom of Fe has been isolated, with half the activity per gram of protein but apparently unchanged in other respects. The total Fe is liberated as inorganic, ferrous iron on acidification or boiling. The enzyme has an amber brown color. A part of this absorption is due to the Fe-protein bond. Reduction by hydrosulfite or by succinate causes the appearance of a difference spectrum characteristic of flavoproteins. Conventional methods of denaturation liberate little or no flavin from the enzyme, but prolonged boiling in acids liberates considerable free flavin, as does digestion with trypsin and chymotrypsin, in accord with observations in Green's laboratory (personal communication). Only a small fraction of the trypsin digest registers as FAD in the D-amino acid oxidase test. Thus, flavin appears to participate in the action of succinic dehydrogenase, but it is extremely tightly bound, and the exact form in which it occurs in the enzyme remains to be determined.

NEUROBLASTOMA IN CHILDHOOD. C. EVERETT KOOP, WILLIAM B. KIESSWETTER, AND ROBERT C. HORN, JR. Surgery 38:272, 1955.

A series of 44 cases of neuroblastoma occurring in infants and children is reported. Of 39 patients coming under observation at least 14 months ago, 12 survive to date. The 14 month interval is considered to be equivalent to the conventional 5 year follow-up period in the adult. The survivors are without clinical evidence of disease despite the fact that many of the tumors were incompletely removed or were known to have metastasized, often to the liver. No patients with bone metastases were among the survivors. The survivals could not be related to radiation treatment or chemotherapy. The chances of clinical "cure" were best in the youngest age groups. Most of the tumors of the surviving patients showed some degree of differentiation. The removal of all or a major portion of a neuroblastoma, even in the presence of metastases, is associated with a better survival rate than when biopsy alone is performed on an "inoperable" tumor.

STUDIES ON THE PERCUTANEOUS ABSORPTION OF FLUDROCORTISONE. C. S. LIVINGOOD, J. S. HILDEBRAND, J. S. KEY, AND R. W. SMITH, JR. A.M.A. Arch. Dermatol. 72:313, 1955.

Percutaneous absorption of fludrocortisone (9a-fluorohydrocortisone) may occur following topical application of the drugs; if the quantity absorbed is sufficient, sodium retention, manifested by decreased urinary sodium excretion, weight gain, and/or edema may be a complication of therapy. Clinical and experimental data in reference to 11 hospitalized patients with various types of dermatitis who were treated with 0.1 percent or 0.2 percent fludrocortisone lotion and/or ointment are presented. Similar data for two ambulatory volunteer subjects with normal skin are included. Absorption is facilitated when the medicament is applied in a lotion vehicle rather than an ointment base. For short-term therapy, a probable "safe" daily topical dose

*From Edsel B. Ford Institute for Medical Research.

of fiudrocortisone is 2-6 mg. in lotion form, and 5-12 mg. in an ointment base; in some patients, with prolonged daily treatment, even these quantities may cause significant sodium retention, especially if applied to the perianal and/or vulvar areas. In general, it seems preferable to avoid the use of fiudrocortisone ointment and lotion in patients who have hypertension, toxemia of pregnancy, congestive heart failure, and nephritis. Patients who are using fludrocortisone topical preparations should be observed at regular intervals and checked for weight gain and edema. The medicament should be discontinued immediately if there is evidence of sodium retention as manifested by significant weight gain and/or edema. Percutaneous absorption of a glucocorticoid producing systemic effects can occur without being detectable by determination of the urinary 17-hydroxycorticosteroid and 17-ketosteroid excretion; the circulating eosinophile count has the same limitation. Clinical experience to date indicates that fludrocortisone is a very effective topical medicament for the treatment of various types of dermatitis; if appropriate precautions are observed, problems resulting from significant sodium retention will be minimal.

ANTIGENICITY OF B-PROPIOLACTONE-INACTIVATED VIRUS VACCINES. GERALD A. LOGRIPPO AND FRANK W. HARTMAN. J. Immunol 75:123, 1955.

The search for a more satisfactory agent in the preparation of inactivated virus vaccines has continued through the years. The physical and chemical agents currently in use are not entirely satisfactory due to the narrow margin of safety between complete virus inactivation and the degree of antigenicity retained. Although the bulk of the virus can be inactivated relatively easily, it is extremely difficult to eliminate the trace quantities of living virus without using larger quantities of the virucidal agent. In obtaining complete inactivation, most agents destroy the virus structure so that little, if any, antigenic response is obtainable. In this respect beta-propiolactone (BPL), a chemical agent not hitherto used in the preparation of vaccines, appears to be superior to formalin and phenol, as a high degree of antigenicity can be maintained even when an excess of the minimal effective virucidal concentration is used. In addition, BPL inactivates completely and irreversibly in 10-15 minutes at 37° C, whereas, formalin and phenol require days under the same conditions, the procedure for preparation of BPL inactivated virus vaccines moreover being simple and rapid. The antigenic response of beta-propiolactone-inactivated virus vaccines in rabbits and mice, as determined by neutralization tests and induceed immunity, show the degree of antigenicity maintained with rabies, eastern equine encephalomyelitis and MM-viruses to be significantly higher than that of either formalin—or phenol-inactivated vaccines. Beta-propiolactone-inactivated MM-virus vaccine in rabbits and rabies virus vaccine in mice produces an antigenic response almost equal to the live virus vaccines. In both instances the amount of drug used was at least 50 percent in excess of that required to inactivate the respective viruses to nondetectable quantities in susceptible animals.

RECENT ADVANCES IN THE TREATMENT OF PERNICIOUS ANEMIA. RAYMOND W. MONTO, JOHN W. REBUCK, AND JAMES T. HOWELL. J. Michigan M. Soc. 54:1101, 1955.

Pernicious anemia is a deficiency disease arising from the failure to absorb 1/1,000,000 of a gram of vitamin B_{12} daily from the gastrointestinal tract. This defect

results in altered systemic cellular metabolism characterized clinically by a macrocytic anemia, gastrointestinal and central nervous system manifestations. When Minot and Murphy announced twenty-five years ago that pernicious anemia could be treated successfully with whole liver, this disease was removed from the category of uniformly fatal refractory anemias. In the therapy of pernicious anemia, we have a potent specific factor, vitamin B_{12}. The transfusion of blood is still important when the degree of anemia is sufficient to produce cardiac insufficiency and, in general, is to be considered when the red blood count is below 1,000,000 cells per cu. mm. Usually 15 micrograms are given each day intramuscularly for one week and twice weekly until full hematological remission is obtained. Aerosol inhalation of crystalline vitamin B_{12} can be demonstrated to produce complete hematological response in pernicious anemia patients. Similar responses result from the inhalation or nasal insufflation of vitamin B_{12} lactose powder. A single application of 150 micrograms of B_{12} crystals on the nasal turbinate mucosa gave a complete remission lasting for three months. In addition to the resolution of the anemia we encountered complete relief from the gastrointestinal symptoms and improvement in the neurological manifestations comparable to parenteral therapy.

LIPOMA OF THE CORPUS CALLOSUM. W. A. Nordin, H. Tesluk, and R. K. Jones. A.M.A. Arch. Neurol. & Psychiat. 74:300, 1955.

A case of lipoma of the corpus callosum treated at Henry Ford Hospital and a summary of cases in the literature since 1946 are presented. Forty-five cases have been reported. Experience with these indicates that there is a distinctive picture seen on plain skull x-rays. When operative removal is attempted the patient seldom survives. Due to their large size, midline location, vascularity, and involvement of the anterior cerebral arteries, complete removal is rarely possible. Those patients explored and only biopsied have better survival records. This case was that of a 16 year old girl who had an excision of a frontal scalp subcutaneous lipoma when 4 months, which recurred at 13. This was excised, and a small stalk was seen to pass through the point of fusion of the anterior fontanel. Later, an attempt to remove the intracranial component was made. Complete removal was impossible. The left anterior cerebral artery was clipped to facilitate exposure of the tumor. The patient died in 26 hours with signs of increasing intracranial pressure. At autopsy, a 5 by 10 by 4 cm. lipoma occupying the midportion of the brain was found displacing the corpus callosum. The splenium of the corpus callosum was absent. The medial surface of both frontal lobes showed softening and petechial hemorrhage, and fresh thrombi were present in both anterior cerebral arteries. Four other cases demonstrating association of lipoma of the corpus callosum with a midline subcutaneous scalp lipoma have been reported. These suggest that some lipomas of the corpus callosum result from inclusion of tissue containing fat-cell precursors within the closing lips of the neural groove and represent a congenital anomaly rather than metaplastic or neoplastic transformation. Many cases have vague symptoms. It appears that occurrence of more severe neurologic signs and symptoms appearing after puberty may be the result of continued slow growth of the fatty tumor after cessation of brain growth.

INTRAMUCOSAL CARCINOMA OF THE ESOPHAGUS. Roger W. O'Gara and Robert C. Horn, Jr. A.M.A. Arch. Path. 60:95, 1955.

A report of an unusual case of carcinoma of the esophagus. During life there were no symptoms directing attention to the esophagus, the patient's complaints being related to cervical lymph node metastases. The clinical diagnosis was squamous cell epithelioma, possibly of parotid salivary gland origin. At autopsy, the only gross abnormality of the esophagus was a tiny ulcer. However, microscopic examination of this area revealed carcinoma and dictated detailed study. The greater part of the esophagus proved to be involved, almost all of the tumor being confined to the mucous membrane and glands. Invasion of the submucosa and the superficial part of the muscle occurred at one point. Metastases were present in the lungs and in cervical, axillary and thoracic lymph nodes.

WHIPPLE'S DISEASE. Robert H. Puite and Henry Tesluck. Am. J. Med. 19:383, 1955.

Four cases of Whipple's disease diagnosed between 1943 and 1954 are presented. Case histories of brothers with proven disease and extensive family history suggesting possible abnormalities in other members is presented. Diagnosis by peripheral node biopsy is proposed. It is concluded that pituitary-adrenal factors have no fundamental role in the etiology or fatal outcome of the disease despite the improvement, at least temporarily, of patients receiving ACTH or corticosteroid therapy. The opinion is expressed that the disease is a hereditary one whose transmission is not greatly different from that seen in the malabsorption syndrome and whose primary defect is probably a metabolic one localized in the intestinal mucosa.

THE MUMPS SKIN TEST AND COMPLEMENT FIXATION TEXT AS A DIAGNOSTIC AID IN SARCOIDOSIS. Edward L. Quinn, David C. Bunch, and Elizabeth M. Yagle. J. Invest. Dermatol. 24:595, 1955.

Investigations have revealed the following: 1) an inability of sarcoid patients to develop and maintain a skin sensitivity to BCG vaccine; 2) the ability to transfer passively tuberculin sensitivity to tuberculin negative patients with sarcoidosis, indicating that the negative tuberculin reaction is not due to anticutins or other inhibiting factors in the skin; 3) a singular lack of cutaneous reactions to oidiomycin, trichphytin, and mumps virus antigen, as well as tuberculin, in patients with sarcoidosis; and 4) failure to develop skin sensitivity in normal fashion after immunization with pertussis agglutinogen, although circulating antibodies appear in normal titres. This latter point consititutes the key in our present studies with the use of the mumps skin test and complement fixation test in sarcoid patients in that we can postulate that patients who have a positive complement fixation test to mumps should usually, in contrast to normal adults, have a negative skin test to the mumps antigen. Seven consecutive patients with sarcoidosis were tested. All had positive complement fixation tests and six of the seven had negative mumps skin test. This indicates a failure of skin sensitivity reaction of 85 percent compared to the expected normal anergic response of 7 percent.

A NEW PTOSIS OPERATION UTILIZING BOTH LEVATOR AND FRONTALIS. ROBERT A. SCHIMEK. A.M.A. Arch Ophth. 54:92, 1955.

Ptosis, or drooping of the upper lid, can usually be corrected by surgery. If there is some muscular power in the levator (the lid muscle that normally elevates the upper lid), it can be shortened and thus strengthened, and the lid lifted into a normal position. Unfortunately, some severe cases of congenital ptosis will have very little or no muscular power in the levator muscle. In such a case, additional use of the frontalis muscle will compensate for any undercorrection that would result from using the very weak levator muscle alone. The following operative procedure combines use of both levator and frontalis muscles. The levator is clamped, dissected from the lid and conjunctiva and split longitudinally. Two incisions are made in the tarsus and above the brow. With a ptosis knife, each tongue of levator is pulled through its tarsal buttonhole and further subcutaneously, up to the frontalis muscle to which it is sutured. This maneuver increases levator power by advancing and thus effectively shortening the levator muscle fibers. Increasing the power of the levator muscle fibers, which are normally used for lid movement, accomplishes the most normal correction possible. Use of levator is the best way to accomplish normal blinking, lid closure and synchronous vertical following movements between the lid and the eye. Additional use of the frontalis compensates for any under correction or lid immobility that might result from use of a paretic levator alone. The frontalis/tarsus connection by levator tendon, rather than a buried suture or a fascia transplant, avoids the risk of infection around foreign material at a later date. Satisfactory results have been obtained in severe congential ptosis with very poor or no levator action using this new operation which combines levator and frontalis utilization.

RESECTION FAILURES IN PULMONARY TUBERCULOSIS. RALPH J. SCHLOSSER AND FRED J. JARVIS. J. Thoracic Surg. 29:335, 1955.

An analysis of the failures in a series of 400 consecutive patients undergoing resection for pulmonary tuberculosis is presented. Detailed study includes the early and late deaths, the readmission and multiple resection groups, and other failures. We feel that this study is helpful in the evaluation of present trends in surgical therapy of pulmonary tuberculosis. Inadequate functional reserve has been a major cause of both early and late death. Whereas major blowout of a bronchial stump indicating insecure closure was responsible for early death in two cases, a third of our late deaths were accountable to empyema with late bronchopleural fistula. The etiology of these late hazards in most cases is felt to stem from seemingly innocuous but persistent pleural fluid. As demonstrated by our readmission and multiple resection group, residual caseous disease is a definite threat to a patient's future. In certain of these patients somewhat greater extension of the initial resection might well have prevented later surgery. Reactivation rather than "spread" is usually the manner of exacerbation of disease following resectional therapy.

EXPERIMENTAL VENTRICULAR SEPTAL DEFECT: The Right Atrial Approach. NICHOLAS P. D. SMYTH, THOMAS GEOGHEGAN, AND CONRAD R. LAM. Surg., Gynec. & Obst. 100:351, 1955.

A method was devised for creating surgical defects in the mid portion of the ventricular septum without damage to the external ventricular wall. A cutting instru-

ment of the cork-borer variety was inserted through the right atrial appendage. The sharp tip of the instrument was guided through the tricuspid valve and beneath the arch of the chordae tendineae of the anterior leaflet and then driven through the septum. The excised plug of septal tissue was removed by suction applied to the lumen of the cutting instrument. This method was used to create septal defects in approximately 100 dogs without producing tricuspid regurgitation or significant conduction disturbances. Photographic recordings were taken with the Hathaway oscillograph of the pressure pulses in the right and left ventricles, the aorta and pulmonary artery and the right atrium. Alterations of the pressure curve contours produced by the defect are illustrated and analyzed. Oxygen studies indicated left to right shunts of 26 to 76 percent through the defects.

LATEROPOSITION OF THE ATRIAL APPENDAGES: A Case Of Levoposition Of The Appendages. NICHOLAS P. D. SMYTH. A.M.A. Arch. Path. 60:259, 1955.

A case is described in which multiple cardiac anomalies were found, the special atrial appendages, both of which lay to the left of the great vessels. In the absence of a generally accepted name for this anomaly, lateroposition of the atrial appendages is suggested as a general term, the two varieties being levoposition and dextroposition of the atrial appendages. The literature on this anomaly, comprising reports on 15 cases of levoposition and 2 cases of dextroposition of the atrial appendages, is reviewed, and the essential features of all the cases are tabulated. The embryology of this anomaly is discussed and a scheme of development suggested for the known variants of this anomaly.

RESECTIONAL SURGERY OF THE ABDOMINAL AORTA: Problems Of Case Selection And Operative Technique. D. EMERICK SZILAGYI, ROGER F. SMITH, AND PAUL R. OVERHULSE. A.M.A. Arch. Surg. 71:491, 1955.

With the background of clinical study of 53 abdominal aortic aneurysms and the experience of 34 resections of lesions of the abdominal aorta (15 aneurysms and 19 aortoiliac segmental occlusions), the problems of aneurysmal case selection and some technical questions in the resectional surgery of the abdominal aorta are discussed. Certain criteria of operability are suggested in the management of abdominal aortic aneurysm. The prognostic significance of the distinction between pure segmental aortoiliac occlusion and segmental aortoiliac occlusion secondary to diffuse arteriosclerosis is stressed. Resection of the entire aortic bifurcation and of all the diseased portions of the common iliac arteries is advised for the treatment of incomplete but advanced aortoiliac occlusion. An extension of the level of resection distalward is recommended in preference to intimectomy in cases where the degree of arterial disease does not permit anastomosis with the intact artery at the common iliac level.

EVALUATION OF DICIDUOUS MOLARS TREATED BY PULPOTOMY AND CALCIUM HYDROXIDE. WILLIAM F. VIA, JR. J. Am. Dent. Assoc. 50:34, 1955.

This investigation was undertaken to evaluate the treatment of primary molars by pulpotomy and calcium hydroxide by studying the postoperative roentgenograms of a number of treated teeth. The procedure followed was to select a sample from the 800 records of pulpotomies on file at the Children's Clinic of the School of Dentistry of the University of Michigan. The sample was limited to deciduous molars in the mandibular arch. Postoperative roentgenograms were secured after sufficient time

had elapsed to determine whether the treatment could be judged. Teeth that were shed less than one year after the pulpotomy were excluded. Also a small number of treated teeth, which were obvious failures from the start. The sample consisted of 102 primary molars. The treatment was judged to have failed in 68.9 percent of the treated teeth. Standard error of this percent was found to be 4.6 percent. Of the 71 teeth on which treatment had failed, 48 exhibited internal resorption with or without periapical involvement. This finding indicates that 68.9 percent of the total teeth on which treatment had failed showed internal resorption. Certain factors which were thought to influence the success or failure of the treatment were subjected to statistical evaluation. These factors included the presence of a preoperative reaction in the tooth, a large area of exposed pulp and injection of anesthetic directly into the pulp tissue. It was found that there was no evidence of any relation between these factors and success or failure, except that which existed through chance alone.

*CRYSTALLINE ALPHA RAY-ACETYLENE REACTION PRODUCTS. JOHN H. L. WATSON. Radiation Res. v. 3, 1955.

Crystals were reported observed in deposits formed by the bombardment of acetylene gas by alpha particles from radon. The crystals were described for acetylene but have been observed also in deposits from CO and CH_2CHCL. The radon was contained within a thin-walled glass bulb, and the deposits were collected directly in the reaction chamber and examined in the electron microscope without manipulation. This is the first observation of crystalline materials in such reaction products. Observation of the usual liquid and quasiliquid droplets was also reported for these materials mounted in this special manner.

*From Edsel B. Ford Institute for Medical Research.

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